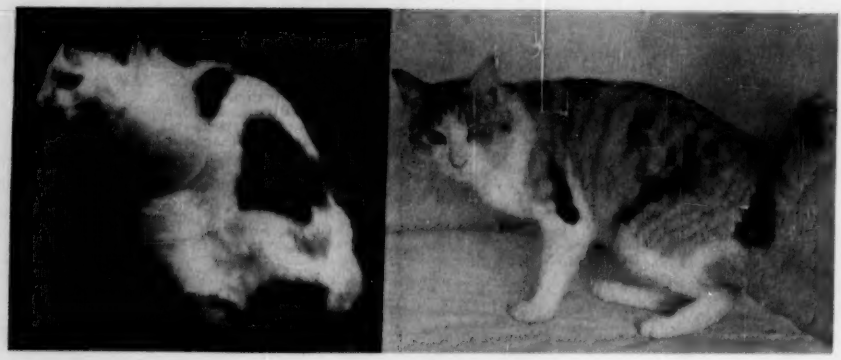
The Journal of HEREDITY



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A New "Luxoid" Mouse

Absence of Radius and Thumb

Cytological Studies of Rust Fungi

X-Ray Induced Asynapsis in Maize

Hazards of Atomic Radiations to Man

Academic Origin of Drosophila Workers

VOLUME 47 NOVEMBER-DECEMBER, 1956 NUMBER 6

The American Genetic Association

An incorporated organization devoted to promoting a knowledge of the laws of heredity and their application to the improvement of plants, animals, and human racial stocks

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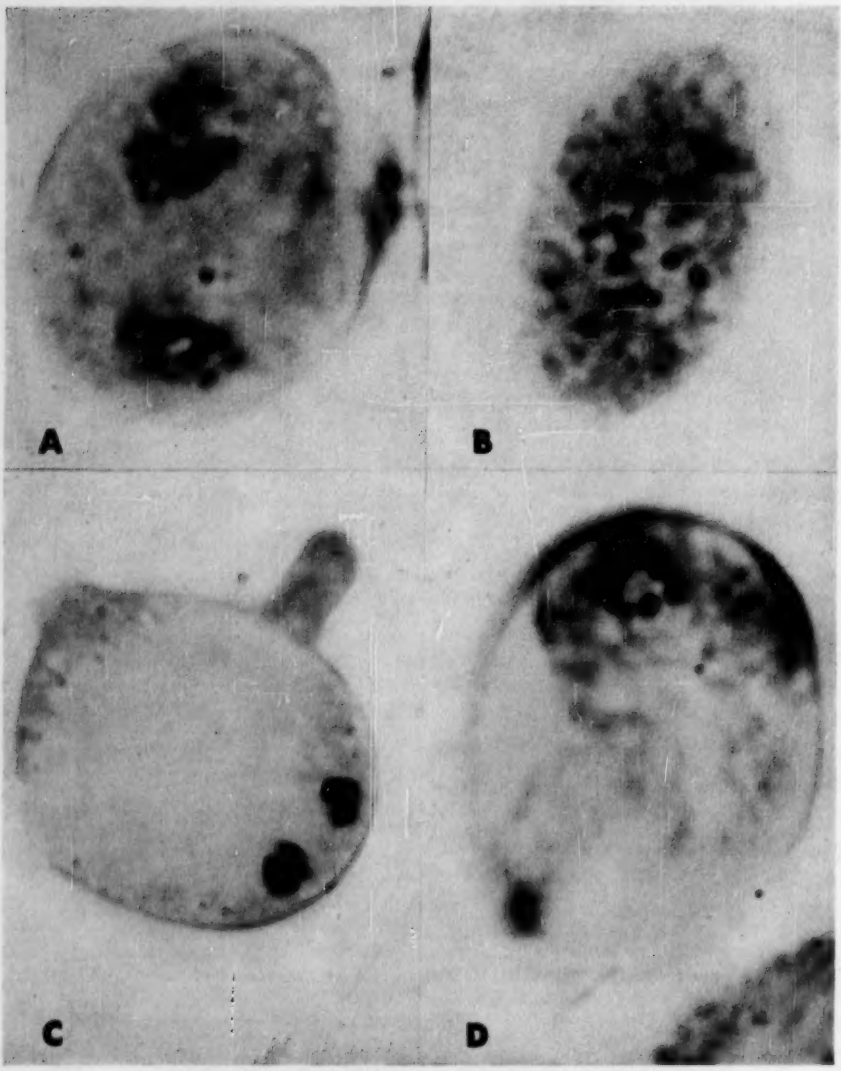

CHROMOSOMES AT METAPHASE AND ANAPHASE

Figure 1

A—Metaphase in *P. xanthii* showing $n = 4$ chromosomes. 4500×. *B*—Anaphase in *P. xanthii* with eight daughter chromosomes migrating to the poles. 4500×. *C*—Metaphase in *P. malvacearum* showing $n = 4$ chromosomes. 3000× *D*—Anaphase in *P. malvacearum* with eight daughter chromosomes migrating to the poles. 3500×.

CYTOLOGICAL STUDIES OF CHROMOSOMES OF RUST FUNGI

III. The Relationship of Chromosome Number to Sexuality in *Puccinia*

R. C. McGINNIS*

VERY few species of the large group of rusts comprising the genus *Puccinia* have been cytologically examined to determine their chromosome number. In *P. arenariae* (Schum) Wint., Lindfors[8] reported a haploid number of $n = 4$. Allen[2] suggested a probable haploid number of five chromosomes for *P. malvacearum* Bert. Later, Savile[11] reported $n = 4$ for *P. malvacearum* as well as for *P. sorghi* Schw. The first two papers in the present series dealt with chromosome numbers in *P. graminis* Pers.[9] and *P. coronata* Corda f. sp. *secalis* Peturs[10]. These species had haploid chromosome numbers of six and three, respectively, and the possibility of a simple polyploid series in the genus with a basic chromosome number of three, was proposed.

P. malvacearum is a homothallic species having only telial and basidial stages in its life cycle[4, 5]. *P. arenariae*, having a similar short cycle is probably homothallic also. If the chromosome numbers in this genus do actually follow definite patterns, then it could be expected that other short cycle species which produce only telia and basidia, should have the same chromosome number. The heterothallic species, characterized by a pycnial stage in the life cycle, might also have a distinctive chromosome pattern as was suggested by preliminary studies on *P. graminis* and *P. coronata*[9, 10]. Consequently, chromosome studies were conducted on a number of homothallic and heterothallic species of *Puccinia* to determine whether chromosome number is related to sexual behavior in this genus.

Materials and Methods

The species studied are presented below, along with their respective hosts from which the collections were made.

Species	*Host*
P. xanthii Schw.	*Xanthium commune* Britt.
P. malvacearum Bert.	*Althaca rosea* (L.) Cav.
P. asteris Duby	*Aster lindleyanus* T. and G.
P. coronata calamagrostis F. and L.	*Calamagrostis montanensis* Scribn.
P. sorghi Schw.	*Zea mays* L.
P. carthami Corda	*Carthamus tinctorius* L.
P. helianthi Schw.	*Helianthus tuberosus* L.

With the exception of *Calamagrostis montanensis* which was collected at Sutherland, Saskatchewan, all the hosts were collected at Winnipeg, Manitoba.

The teliospores were induced to germinate, and the discharged sporidia were collected on microscope slides for cytological examination. Since meiosis occurs in the promycelia of the teliospores just prior to sporidial formation, the sporidia are haploid, and consequently the studies herein reported are concerned with the haploid phase of these species.

All preparations were stained with 2 percent orcein in 60 percent acetic acid, the formula used so successfully by Singleton[12] on *Neurospora*. This solution was found to be more satisfactory than the weaker concentration (1 percent orcein in 45 percent acetic acid) used in previous studies[9, 10]. Deeply stained nuclei and chromosomes were obtained in most of the sporidia while the cytoplasm remained relatively clear. As a matter of convenience some of the slides were fixed and stored in 3:1 alcohol-acetic acid solution. The rest of the slides were stained directly. These two methods did not differ appreciably in their effectiveness.

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Results

With the exception of *P. helianthi*, which will be discussed later, all species studied were very similar in behavior with respect to basidiospore germination and nuclear division. In general, one nuclear division preceded germ tube formation, but occasionally two or more divisions occurred before spore germination (Figure 2*B*). Occasionally germination preceded mitotic division.

Homothallic species—P. malvacearum, P. xanthii and P. asteris

Many thousands of spores were critically examined, and it is estimated that over 100 spores of each species were observed wherein well defined chromosomes at metaphase or anaphase could be accurately counted (Figures 1*A-D* and 2*A*). From these observations, there is conclusive evidence that each of these species has four haploid chromosomes. Thus the haploid number reported by Saville[11] for *P. malvacearum* is confirmed in this study. At metaphase, in all three species, the chromosomes were about 0.75 to 1.0μ in length while at anaphase they were much reduced in size and measured about 0.5μ in each dimension. So far as could be determined all four chromosomes in each of the species were of approximately the same size. There did not appear to be two chromosomes slightly larger than the other two at anaphase as reported by Saville[11] for *P. malvacearum*. However, the metaphase configuration was often in the form of a square, (Figures 1*A* and 2*A*)), again confirming Savile's observations.

One phenomenon which warrants mention is the occurrence of end-to-end union of chromosomes to form complete rings (Figure 2*C*). Although chromosome union sometimes results from fixation in acetic acid-alcohol solutions, it seems unlikely that this could fully account for their presence in this study since they were observed in both fixed and unfixed material. A fairly high frequency of such configurations was observed in the three short cycle species indicating that they may constitute a normal stage in many divisions. Frequently one, and sometimes two nuclei of a sporidium behaved in this manner. It seems possible that the chromosome unions observed in this study may be similar to those observed in *P. graminis*[9] although in the case of *P. graminis* the chromosomes failed to complete the ring. In preliminary studies of *P. minussensis* Thum. and *Melampsora* lini (Pers.) Lev. (unpublished data) ring configurations were also observed. Consequently, it can be postulated that such chromosome unions are not peculiar to any one species, or even genus, but may be common to the rusts as a whole. Their significance is unknown at the present time.

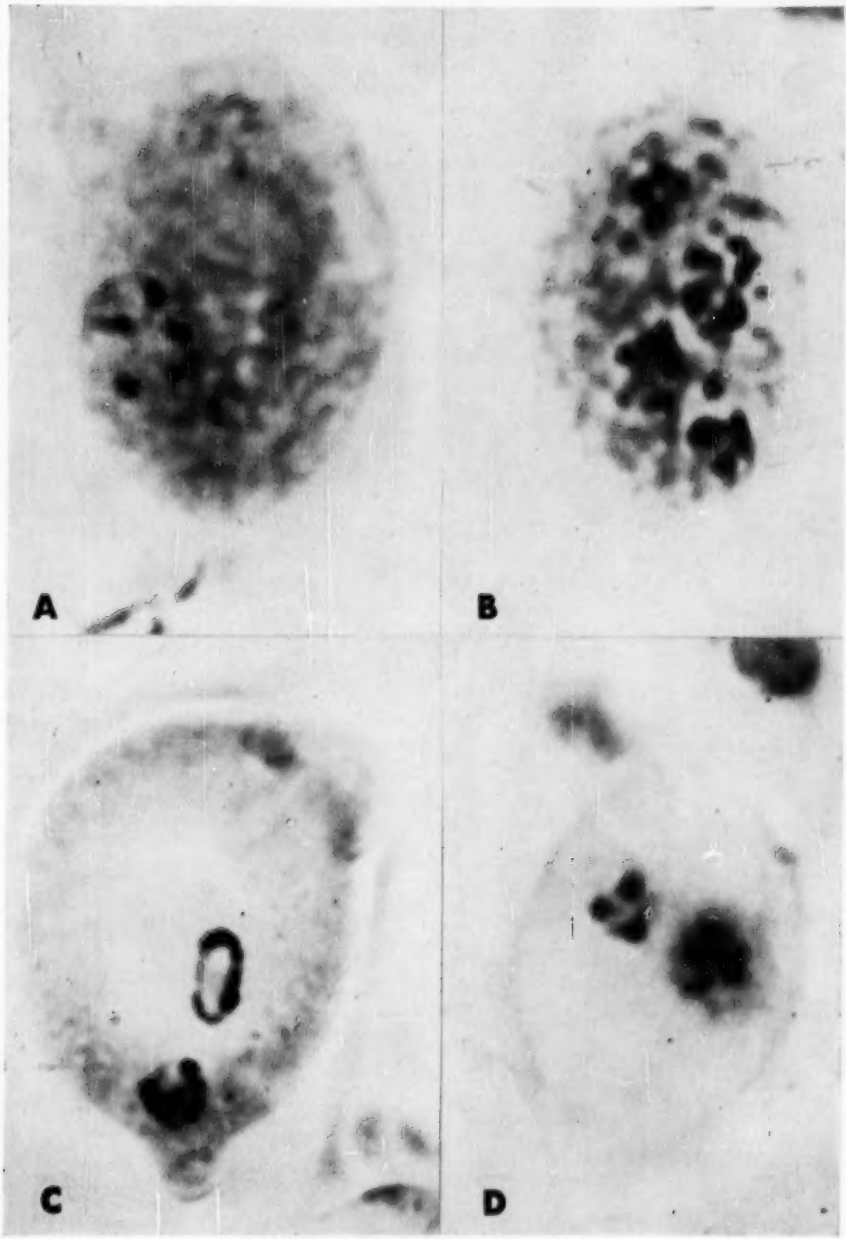
Heterothallic species—P. coronata calamagrostis, P. carthami, P. sorghi and P. helianthi

P. coronata calamagrostis proved to have $n = 3$ chromosomes (Figure 2*D*), therein resembling *P. coronata secalis*[10]. The remaining three species, *P. carthami*, *P. sorghi* and *P. helianthi*, each had $n = 6$ chromosomes (Figure 3*A-C*). No previous reports of chromosome counts are known for *P. carthami* and *P. helianthi*. The haploid number of six chromosomes found in *P. sorghi* in this study does not agree with Savile's count of $n = 4$ [11].

Mitosis in the basidiospores of *P. helianthi* was unique in several respects. The first mitotic division appeared to proceed normally and occasionally the chromosomes condensed at metaphase of the second mitotic division as in normal divisions (Figure 3*C*). Most often, however, the chromosomes appeared as stringy masses of unusually large size (Figure 3*D*). Anaphase was never observed in such divisions. Instead, the chromosomes seemed to retain their individuality, elongate even more and migrate into the germ tube as long chromatic strands (Figure 3*E*). Whether the nuclei passed into the germ tube singly or together was apparently due to chance alone. In some instances the two nuclei were in such close proximity during migration that their individuality was no longer distinguishable (Figure 3*F*). This type of nuclear behavior was confined only to *P. helianthi* of the species studied. In the other species the nuclei appeared to be fully condensed prior to migration, and although elongation of the nuclei occurred during migration into the germ tube, it was much less exaggerated than in *P. helianthi*. Also in the other species the nuclei migrated as distinct bodies rather than as chromatin strands.

Discussion

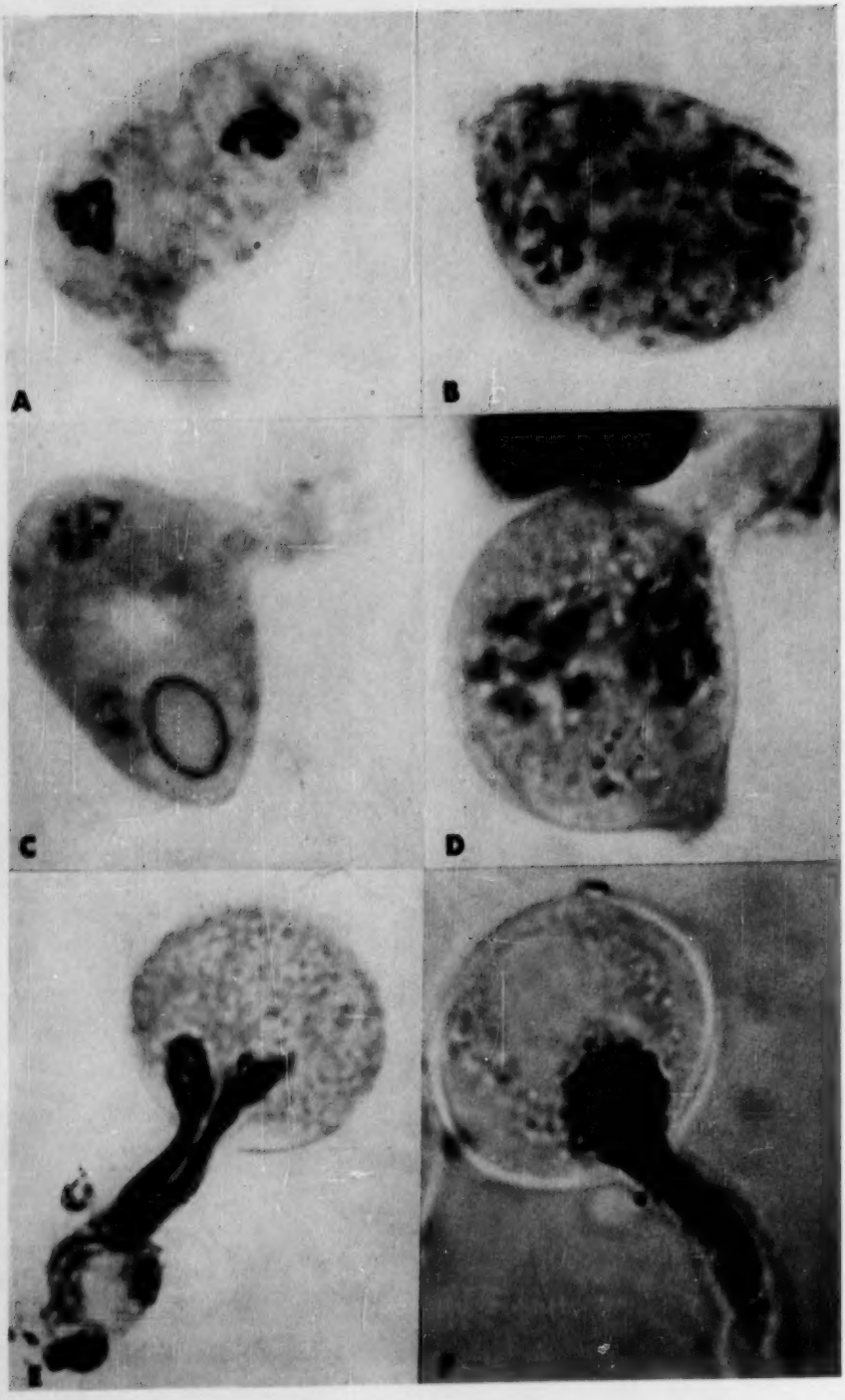
The existence of species of *Puccinia* with chromosome numbers of $n = 3$, $n = 4$, and $n = 6$, respectively, is of considerable interest from the standpoint of the possible role of polyploidy in the evolution of the species in this genus. It is possible that species with $n = 3$ are true diploids and could have become reduplicated for one chromosome to produce species with $n = 4$ during the course of evolution. It is equally possible that the basic chromosome number for the genus is two, and that species with $n = 3$ originated from reduplication of one chromosome in the hypothetical original $n = 2$ diploid. On this assumption, species with $n = 4$ would in reality be tetraploids and those with $n = 6$ hexaploids. A third possibility exists—that of two distinct basic chromosome numbers in the genus, $n = 2$ (or 4) and $n = 3$. In this case, species with $n = 3$ would be true diploids while species with $n = 4$ could be either diploid or tetraploid. Species with $n = 6$ could theoretically fit into either scheme. If they belong to the group having a basic number of 3, they would be tetraploids, but if they were included in the $n = 2$ group, they would be hexaploids. On the basis of sexual behavior, it seems most likely that $n = 6$ species belong to the former group.



CHROMOSOMES OF FOUR SPECIES

Figure 2

A—Metaphase in *P. asteris* showing $n = 4$ chromosomes. 3900×. *B*—Ungerminated sporidium of *P. xanthii* with four dividing nuclei. 4500×. *C*—Ring configuration from end-to-end union of chromosomes in *P. malvacearum*. 3000×. *D*—Metaphase in *P. coronata calamagrostis* showing $n = 3$ chromosomes.


A
B
C
D

It is interesting to note that the species for which chromosome numbers have been determined can be divided into two groups on the basis of sexual behavior and chromosome number as summarized in Table I. *P. graminis*, *P. sorghi* and *P. helianthi* are known to be heterothallic[3,6,7] and have all spore stages in their life cycles. Similarly *P. coronata secalis* and *P. coronata calamagrostis* are presumed to be heterothallic since their sexual behavior is similar to that of *P. coronata avenae* Erikss. and Henn. which Allen[1] showed to be heterothallic. These rusts also have all spore stages in their life cycle. Although *P. carthami* omits the aecial stage in its life cycle, Brown (unpublished data) has demonstrated heterothallism in this species. On the other hand, *P. malvacearum* is homothallic[4,5] as is *P. xanthii*[5] while *P. asteris* is presumed to be homothallic (A. M. Brown, personal communication). *P. arenariae*, having a life cycle similar to that of the homothallic species, is probably homothallic. Consequently, from the limited evidence available at present, there is an indication that heterothallism and homothallism in *Puccinia* may be associated with specific chromosome numbers. The heterothallic rusts apparently comprise a polyploid series of $n = 3$ and $n = 6$, while the homothallic rusts comprise a group having $n = 4$ chromosomes.

TABLE I. Species of *Puccinia* classified according to chromosome number and sexuality

Haploid chromosome number	Sexuality	
	Homothallic	Heterothallic
4	*P. malvacearum* *P. asteris* *P. xanthii* *P. arenariae*	
3		*P. coronata secalis* *P. coronata calamagrostis*
6		*P. graminis* *P. helianthi* *P. sorghi* *P. carthami*

Summary

Cytological studies were conducted on germinating sporidia of three homothallic (short cycle) rusts, *Puccinia xanthii* Schw., *P. malvacearum* Bert., and *P. asteris* Duby to determine their chromosome number. At metaphase and anaphase of mitosis, a haploid number of four chromosomes was observed in each of these species. In many cells the chromosomes were joined end-to-end to form rings. The significance of the ring configurations is not known at present. Studies were also made on four heterothallic (long cycle) species, *P. coronata* Corda *calamagrostis* F. and L., *P. sorghi* Schw., *P. carthami* Corda and *P. helianthi* Schw. *P. coronata calamagrostis* was found to have $n = 3$ chromosomes while the latter three species each had $n = 6$. It is suggested that sexual behavior may be dependent on chromosome number since all the homothallic species studied thus far have $n = 4$ chromosomes, while the heterothallic species have either $n = 3$ or $n = 6$ chromosomes.

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CHROMOSOMES OF THREE SPECIES

Figure 3

← *A*—Metaphase in *P. carthami* showing $n = 6$ chromosomes. 4000×. *B*—Metaphase in *P. sorghi* showing $n = 6$ chromosomes. 4000×. *C*—Metphase in *P. helianthi* showing $n = 6$ chromosomes. The chromosomes have condensed as in normal divisions. 3800×. *D*—Metaphase in *P. helianthi*. The six chromosomes in the left hand nucleus appear large and stringy. The group of chromosomes on the right are migrating toward the germ tube without forming a nucleus or even undergoing anaphase. 4500×. *E* and *F*—Nuclear migration of *P. helianthi*. In *E*, the two nuclei are well separated and the chromatin strands (possibly from individual chromosomes) are quite distinct. In *F*, the two nuclei are so intimately associated that their individuality is lost. 3800×.

THE HAZARDS OF ATOMIC RADIATIONS TO MAN

British and American Reports*

BENTLEY GLASS†

ON June 12, by very nice timing, the Committees of the National Academy of Sciences of the United States which had been appointed to study the effects on human populations of the actual and foreseeable dangers of ionizing radiations, and likewise the Committee of the British Medical Council appointed to the same end simultaneously released their reports. There were six separate American committees, designated to consider respectively the areas of genetics, pathology, meteorology, oceanography and fisheries, agriculture and food supplies, and the disposal and dispersal of radioactive wastes. The single British committee did not undertake to consider all of these aspects, but concentrated on the genetical and pathological implications, with a panel for each. In undertaking to collate and compare the two reports, it is consequently most significant to focus on (*a*) the effects of radiation on the health of the exposed individual, and (*b*) the genetic consequences to the individual and his descendants as well as to the population as a whole. The remaining aspects considered by the American committees will be left to another occasion.

Inasmuch as both reports were prepared for the general reader, each of them contains a great deal of explanatory material that is of an elementary nature to radiation biologists, although the physical explanations may be necessary for some biologists, and the genetical explanations for some physicists. In style the American report, in particular that part deriving from the geneticists, is more popular; the British, more comprehensive. Either of them should be intelligible not only to scientists, but also to careful and intelligent nonscientist readers. The American committees are scheduled to make further, more technical reports; and in fact, that of the Pathology Committee has already been distributed. Both reports are available for general distribution.‡

The Effects of Radiation on the Health of the Individual

The information for the appraisal of the pathological effects of ionizing radiations comes from four main sources: radiotherapeutic experience; occupational experience, including the consequences of accident; experience from atomic bomb explosions; and experimental studies of the acute and chronic effects produced on animals. The first of these categories includes not only excessive exposures to X-rays and radium, but also the effects of therapeutic internal use of radioactive isotopes. Under occupational exposures, the American committee includes those of cyclotron workers (not specifically mentioned by the British committee), while the British committee stresses the experience of painters of luminous dials for watches and clocks and of miners working radioactive ores, in addition to medical radiological workers. The American report makes use of the medical data collected on the Mar-

*This article originally appeared in the *Bulletin of the Atomic Scientists*, October 1956, and is published here in full by permission of the author and of the *Bulletin of the Atomic Scientists*.

†Department of Biology, Johns Hopkins University, Baltimore, Maryland. Dr. Glass is a member of the committee which prepared the American Report.

‡American Report: *The Biological Effects of Atomic Radiation*, National Academy of Sciences—National Research Council, Washington, D. C., $1.00; British Report: *The Hazards to Man of Nuclear and Allied Radiations*, Her Majesty's Stationery Office, London, 5s. 6d.

shall Islanders who were unwittingly exposed to fall-out after an experimental test explosion, in addition to the data from the Atomic Bomb Casualty Commission's study of the irradiated populations of Hiroshima and Nagasaki, on which both reports rely heavily.

The British report succinctly summarizes the kinds of factors affecting the severity of radiation injury. These are: the dose of radiation received; the extent of the body irradiated; the part of the body irradiated; the type of radiation; the age of the exposed individual; and the frequency of radiation effects. As is well known, for equal doses of radiation in r units or equivalents, whole-body radiation produces far more severe consequences than irradiation of a part, and irradiation of the trunk, especially the abdominal region, produces far more damage than irradiation of a limb. Neutrons are about equal to X-rays and gamma rays in producing acute radiation sickness, but some 10 times more potent in causing cataract in the lens of the eye. Children are more likely than adults to develop reactions, for equivalent doses received. As to the frequency effects, a single dose within a short interval of time is far more damaging than the same dose spread out over a long period. In fact, there is a threshold below which the acute effects of single doses are not evident, and the increase in effect with increasing doses is greater than linear proportionality. It is not clear whether this applies to the shortening of life from chronic radiation. Both reports agree that a whole-body dose of about 500 r (American report: 400-600 r) would cause acute radiation sickness in all the exposed persons and would cause the death of half of them. A whole-body dose of 100 r would probably cause sickness in not more than 15 percent, and only a few deaths; and a single whole-body dose of 50 r would very rarely produce acute illness (British report).

The British report deals most extensively with the delayed effects of radiation, especially in producing leukemia and cancer. The American report, on the other hand, emphasizes the differing sensitivity of different tissues, and organizes the information about acute and delayed effects tissue by tissue: blood and blood-forming tissues; intestinal tract; skin; bone; lung; thyroid; eye; reproductive organs (gonads); central nervous system; and effects on embryos. The British report in the end covers the same ground by means of sections on the effects of exposure to radiation during pregnancy, and on the effect upon fertility.

Effects on the blood and blood-forming organs are extremely important. A depression in the numbers of red cells and platelets, and particularly of the white cells, may be expected after a severe dose of whole-body irradiation. The loss of white cells may occur at a level of chronic radiation even as low as 1 r per week (British report). Damage to the bone-marrow may lead to an aplastic anemia, in which red cells are not sufficiently replaced; but the most striking of the blood effects is leukemia, which may follow either a single exposure or chronic exposures.

The Britsh report points out that the incidence of leukemia in the irradiated populations of Hiroshima and Nagasaki is about four times that of the selected control population (for eight years, 1947-54, 59 proven and four suspected cases in the former city; 32 proven and 10 suspected in the latter). Among survivors less than 1,000 meters from the hypocenter of the Hiroshima explosion, there were 15 cases in a number so small that no cases would be expected in an unirradiated population of the same size and composition. The average length of time from explosion of the bomb to the first appearance of symptoms was about six years, and the annual incidence has remained approximately constant through the eighth year.

Even more significant relations between ionizing radiations and leukemia are shown by data given in the British report for a study of heavily irradiated persons with ankylosing spondylitis. The survey included 13,352 patients with

ankylosing spondylitis who were treated with X-rays during the period 1935-54; and about 400 untreated patients with the same disease. In the irradiated group the incidence of leukemia was 0.33 percent, a rate about 10 times the general incidence. No cases occurred in the 400 unirradiated patients. There was a striking increase in frequency with increasing dose of radiation, but it cannot be stated at present whether that relation is rectilinear or curvilinear. The average length of time between first exposure to X-rays and diagnosis of leukemia was six years. The British report also mentions a reported rise of about nine times for deaths from leukemia among American radiologists, as compared with other American physicians.

The British report discusses in some detail the origin of cancer of the lungs from the inhalation of radon, as seen among the pitchblende miners of Schneeberg and Joachimsthal, nearly half of whom died of lung cancer in the days before the hazard was recognized and international safety standards were established. The average latent period in those miners was about 17 years, and the estimated dose to the lungs about equivalent to 1,000 r. There is no evidence that external irradiation by X-rays or gamma rays will cause lung tumors in man. Cancer of the bones and joints was induced in a number of workers who were employed in painting numerals on luminous watch and clock dials, and who customarily moistened their brushes between their lips. Swallowing various amounts of radium, along with thorium disintegration products, which tend to concentrate in bone, they died within three to upwards of 15 years afterwards. The earlier deaths were from severe anemia, hemorrhages, and infections, particularly of the jaw bones, the later ones from cancer of the bones. The ingestion of radioactive strontium (Sr^{90} is the long-lived isotope) would have similar effects. So far, no one has developed radiation-induced bone cancer who carried less than 3.6 microcuries of radium alone in his body; or less than 0.52 microcuries of radium with some mesothorium or radiothorium; but cystic changes in bone may occur with as little as 0.4 microcuries of radium alone. These figures should be compared with the maximum permissible level for body radium alone, which was set by the International Commission on Radiological Protection at 0.1 microcurie. Cancer of the skin, with very long latent periods after exposure to the radiation, occurred in a number of radiologists in the early part of the century, and also in patients who had been injudiciously exposed to X-rays for the treatment of acne or the removal of facial hair (B.R.).

Both leukemia and cancer have been reported among young children X-rayed, often early in infancy, for suspected enlargement of the thymus gland, or for bronchitis, infected tonsils and adenoids, or enlarged neck glands. Cancer of the thyroid occurred after an average latent period of seven years in a series of children irradiated for the first of the reasons given, and in one case after a recorded dose of no more than 250 r (B.R.).

Cataract of the lens has been found not only among the cyclotron workers exposed to neutron radiation, but also in Hiroshima and Nagasaki. Among 98 cases at Hiroshima, 85 occurred in persons within 1,000 meters of the explosion center, where they would have received neutron as well as gamma radiation (B.R.).

Skin damage, including destruction of the sebaceous glands, may be permanent with doses of 1,500 r or more (B.R.). The British report states that a dose of the order of 300-400 r will cause a temporary loss of hair, but the Marshall Islanders of Rongelap who received an estimated 175 r whole-body irradiation from fall-out, suffered temporary loss of hair and rather marked skin lesions (B.R.). It is likely that particular areas of the skin in these instances received a much heavier dose from direct contact with radioactive particles. Permanent loss of hair will follow heavy dosages (B.R.).

Whereas the British report has very little to say about shortening of the life span by irradiation, except that there is evidence from animal experimentation, the American report emphasizes this effect. Figures are given for a study of radiologists who may have received from very little up to about 1,000 r during their occupational lives, to show a shortening of life by about five years (60.5 years as against 65.6 or 65.7 years), in comparison both with other physicians and with the general population. Specialists having some exposure to radiation, such as dermatologists or urologists, fall midway between.

As to the effect upon fertility, it is well known that irradiation will produce temporary and even permanent sterility. In men, 500 r to the testes would probably produce permanent sterility (B.R.); but the Marshall Islanders and the Japanese of Hiroshima and Nagasaki, as well as certain accident cases, show that doses up to 40-50 percent of the whole-body lethal dose do not sterilize permanently (A.R.). The dose to the ovaries required to produce the same effect probably is about the same in a young woman, and becomes less with advancing age (B.R.).

Heavy doses of radiation to a fetus in utero will cause a miscarriage or abortion. The frequencies of abortion and stillbirth among pregnant women in the two Japanese cities were related inversely to distance from the center of explosion (B.R.). Highly specific malformations will occur in the fetus, depending on the stage of development at the time of exposure. At certain critical stages even low doses may have a serious result (A.R.). Microcephaly is particularly striking in those irradiated between the twelfth and eighteenth weeks of pregnancy, and may lead to slight or extreme mental impairment (B.R.).

The harmful effects of strontium-90 have already been mentioned. These are owing in part to its long half-life (10,000 days) and in part to its chemical and metabolic similarity to calcium. Because of the latter fact, it tends, once ingested, to concentrate in the bones and to stay there indefinitely. The American report calls particular attention to the danger of strontium-90 contamination of forage and food supplies from radioactive fallout. At the present time a continuing and worldwide check is being made of the accumulation of radioactive strontium in human and animal bones. Some accumulation, up to 0.001 microcurie, has been found. This is .001 of the permissible dose, and if maintained throughout life would result in a dose of 0.2 rep (r equivalent) to the skeleton. So far, the danger does not appear very great, but it is certainly an aspect of the situation that must be closely watched. A safe worldwide allowance might be a strontium load amounting to one-tenth of the present permissible dose, or 20 rep per lifetime *to the skeleton* (the dose to the gonads from this source would be very much less; see following section). Visible skeletal changes have been reported only after hundreds of accumulated rep, and tumors only after 1,500 rep or more.

The Genetic Effects of Radiation

Both British and American reports stress that, upon the basis of all existing genetical information, it cannot be assumed that any dose whatsoever of ionizing radiation is without genetic effect. That is to say, there is no threshold for mutation of the hereditary material. Hence what is significant is the total dose of ionizing radiation accumulated by the germ cells of an individual from conception to conception, an average, both committees assume, of approximately 30 years. From the genetical point of view, it does not matter whether a given dose is in a few large amounts or in many very small ones. From the standpoint of the population it does not matter whether it is administered to many individuals or a few. It is the *total* dose to which the number of induced mutations is proportional.

The American report stresses the fact that there is no disagreement among geneticists as to fundamental conclusions in this area, and the British report by its very agreement fortifies that statement—for there is indeed no fundamental, and scarcely any minor, disagreement between them. For example, although it is well known that ionizing radiations will produce chromosome breakage and structural rearrangement, the British group states that these, because of their production mainly by large single doses of radiation and their speedy elimination, are "likely to be of comparatively little importance among the radiation hazards

to man." The American committee, by omitting even to discuss this category of mutations and by restricting its considerations to *gene* mutations, implicitly adopts the same point of view. Both groups warn that the majority of gene mutations, at least of those which produce obvious or just detectable effects, will be deleterious as a natural consequence of the past action of natural selection, which has culled the mutations of the past and preserved in the population those which are most advantageous in respect to survival to the reproductive age and in respect to fertility and fecundity. Both groups point out the existence of spontaneous mutations, most of which are probably only in part caused by natural "background" radiation (cosmic rays, radioactive matter in the surroundings, radioactive matter ingested and incorporated in the body); and both groups point out that there is a pool of all kinds of possible mutations in the genetic material of each species, the frequency of a particular kind of harmful gene being determined by an equilibrium between its production through mutation and its elimination through selection. Both groups emphasize that there is no "safe," that is, genetically ineffective, rate of radiation. Every dose to the gonads, no matter how minute, adds its bit to the quota of mutations if it is administered to cells that actually participate in producing a new generation. Both groups take pains to point out that the fact that evolution is based on the occurrence of mutations and their incorporation into the composition of a species does not alter the general harmfulness of an increase in the mutation rate. For it is only the action of natural selection on whatever combinations of genes occur, including those with an occasional helpful mutation, that promotes successful adaptation, and every success is accompanied by much genetic damage and loss on the part of the unsuccessful. The consensus is that evolution "has occurred by a succession of small variations from the average" (B.R.), and of these the human population already has, as a result of its past and present mutation rates, "a large enough total supply of favorable, partially favorable, and potentially favorable mutations" (A.R.).

In one significant matter the two groups differ in emphasis. Whereas the British report, although recognizing the existence of large numbers of mutations intergrading between the strictly dominant and the strictly recessive in type, nevertheless deals chiefly with the genetic damage done by representative dominant or homozygous recessive genes, the American report emphasizes the "heterozygous damage" done by so-called recessive genes which nonetheless produce a small but significant amount of harm (shortening of length of life or reduction in fertility) when inherited from a single parent. Thus, in the case of the Japanese of Hiroshima, strictly recessive mutations which were induced would be manifested only after many generations, whenever ultimately two carriers of the mutant gene happened to mate and produce a homozygous child, that is, one with two doses of the gene. But if there is any degree of heterozygous damage by the mutant gene, it applies to many more individuals, indeed to every one who carries the gene at all.

The American report points out that there are at least three aspects to be considered in the estimation of genetic damage from mutation. First is the risk to the direct offspring and later descendants of persons who receive a substantially larger exposure than the average for the entire population. Second is the effect of the average dose on the whole population in terms of the increased number of harmful characteristics. Third is the risk of upsetting the balance between the death rate and the birth rate within the population to such an extent that the population as a whole "would decline and eventually perish." About this third risk the British report does not speak, and much the most weight is given by it to a consideration of the second of the three effects. The minimizing of the first is quite in line with the nonconsideration of "heterozygous damage."

In estimating the existing and foreseeable levels of exposure to radiation, the two reports are in remarkably good agreement. The 30-year total accumulated dose to the reproductive organs from the natural background is estimated at 4.3 r by the American committee, at 3 r by the British. The higher average altitude of North America than of Great Britain is almost enough to account for this difference, because of the increase of cosmic rays with altitude. In some places in the United States the background amounts to 5.5 r.

There is emphatic agreement that the largest contribution to the exposure of present populations both in Great Britain and in the United States is from X-rays used for diagnostic and therapeutic purposes. The American report estimates this amount at 3 r to the gonads over the 30-year average reproductive lifetime; the British report estimates diagnostic radiation as amounting to at least 22 percent of the background radiation, and perhaps much more, plus an unknown amount for the therapeutic radiation of individuals still to have children. Other sources of man-made irradiation include X-ray fluoroscopes for shoefitting, luminous dials of watches and clocks, and television sets. The irradiation to the gonads from these sources is minor or negligible in comparison with the exposure to medical and dental X-rays; but it is interesting that the calculated 30-year dose to the gonads from a wristwatch is 0.3 r (B.R.), which is larger than the estimated 30-year dose from the fully built-up radioactivity resulting from fall-out if both ordinary and thermonuclear bombs continue to be exploded at the same rate as during the past few years. This 30-year dose from fall-out is estimated for Great Britain to be 0.26 r, for the United States to

be 0.1 r, with a range of uncertainty from 0.02 r to 0.5 r. The occupational exposures of medical and dental workers, persons in industry, and workers in atomic energy installations affect a small minority of the population and according to the British add up to only 1.7 percent of the natural background exposure.

According to the British report, therefore, the present exposure to ionizing radiations amounts to approximately 25 percent of the natural background radiation. The American committee, estimating medical and dental exposures at a higher figure—which may represent a real difference between the British and American populations—concludes that the total exposure to artificial sources is at present not much less than the natural background.

In attempting to assess the harmfulness of the radiation-induced mutations which must result from the additional exposure to radiation, the American committee adopted three methods. First, one may say: "Any radiation is genetically undesirable . . . and the genetic harm is proportional to the total dose." Though undeniably true, this affords no baseline for comparison. A dose of $2X$ is twice as harmful as a dose X, but we do not know what amount of harm is done by X.

The second method, also adopted by the British committee, is to use the spontaneous mutation rate as the criterion. Spontaneous mutations at present produce a certain amount of genetic damage, which may be regarded as a sort of "normal" burden on society. If, then, we estimate the "doubling" dose which would just double the spontaneous mutation rate, we can calculate what this would do to the frequency of each harmful hereditary trait in the course of a succession of generations. To do this requires a knowledge of both the spontaneous and induced human mutation rates. Only a few of the former have been estimated; the British report in an Appendix gives the rates of 15 of them, ranging from 4 to 95×10^{-6}, but it cannot be said how representative a sample of human genes these really are, and there is considerable uncertainty in many of the calculations. No radiation-induced mutation rates for mankind are known, so here the data from experimental animals, especially the fruit fly *Drosophila* and the mouse, must serve. The British report devotes considerable space to considerations relevant to the estimation of the doubling dose. If we assume the radiation-induced fraction of the spontaneous mutations in man to be two percent (as in fruit flies, corrected for the differences in length of generation and of spontaneous mutation rates between man and fruit fly), or as 20 percent, as in the mouse, we obtain estimates of the doubling dose of five or 50 times the natural background radiation. The doubling dose thus falls between 15 r and 150 r. The American report sets the lower limit at about 5 r, the amount of the background radiation, and the upper limit at 150 r, on the basis of the work with mice and the Japanese experience. Doubling doses for other organisms, plants and animals alike, fall mostly between 25 r and 60 r (B.R.). Both reports set the best estimate, taking all grounds into consideration, as falling between 30 r and 80 r.

The effects of doubling the over-all mutation rate upon the frequency of various undesirable traits is illustrated in each report by various examples. At present about four to five percent of all live births in the United States represent defects of a tangible sort such as "mental defects, epilepsy, congenital malformations, neuromuscular defects, hematological and endocrine defects, defects in vision or hearing, cutaneous and skeletal defects, or defacts in the gastrointestinal or genito-urinary tracts . . . . of all of these, perhaps about half—or two percent of the total live births—have a simple genetic origin . . ." (A.R.). A doubling dose continued indefinitely would therefore lead to an ultimate doubling of the frequency of such hereditary defects in the population, or, in 100 million births, about four million children with such genetic defects. "Perhaps 10 percent of the increase, or 200,000 new instances of tangible inherited defect, would occur in the first generation" (A.R.). A dose of 10 r per generation would be expected to produce about 50,000 new cases in the first generation and ultimately about 500,000 additional cases per generation.

The British report supplies more detail in regard to the rapidity with which this ultimate equilibrium is approached in different modes of inheritance. For a dominant gene such as that responsible for achondroplasia, a type of dwarfism, the incidence of which is one in 9,400 and which is marked by low fertility, a doubling of the mutation rate for a single generation would produce an 80 percent rise in frequency in the first generation, followed by a rapid decline, within five or six generations, to the normal incidence. A permanent doubling of the mutation rate would double the incidence within three or four generations. The frequency of a sex-linked trait such as hemophilia would be modified in the same way, but less abruptly. Doubling the mutation rate for one generation would produce only a 29 percent increase in frequency in the first generation, and a permanent doubling would bring about an increase of 90 percent in about six generations. The remaining increase, to double the original incidence, would take place more slowly. A typical simple recessive trait, such as phenylketonuria, which is associated with severe mental defect, and which has at present an incidence of about one in 40,000, would be increased in frequency by only one percent in the generation immediately following a doubling of the mutation rate. If the mutation rate were permanently doubled, it would take more than 50 generations to increase the incidence by 50 percent, and a great many more to attain the eventual doubling of the frequency.

Another analysis in the British report gives the effect of doubling the mutation rate on broad categories of disease, including severe mental defect, mental illness, blindness, and neonatal deaths, stillbirths, and congenital malformations. In Great Britain the incidence of serious mental defect among those surviving infancy is about one in 500, of which dominant hereditary conditions make up some four percent. It is estimated that there would be an over-all increase of three percent in the first generation following a doubling of the mutation rate, i.e., 1,500 additional cases to add to the 50,000 in 20 million births now requiring institutional care. A permanent doubling would of course eventually double the burden on the population. In Great Britain there were in 1954 approximately 63,000 cases of schizophrenia and 31,000 cases of manic-depressive psychosis, the two diseases together making up about half of all mental illnesses. There is evidence of strong hereditary factors in each of these illnesses. Doubling the mutation rate would perhaps raise the incidence of schizophrenia by one percent and of manic-depressive psychosis by 1.4 percent. In the first generation this would produce 200 chronically incapacitated schizophrenics and a like number of chronically incapacitated manic-depressives in 20 million births. The number of extra patients needing some psychiatric care would be five to 10 times as great. A permanent doubling would have in each succeeding generation about the same additional effect, until the eventual doubling of the frequency was attained. About three-fourths of all congenital or early blindness is thought to be hereditary. A doubling of the mutation rate would produce in the first generation at least 80 additional cases of aniridia, 80 cases of microphthalmos, and 560 cases of retinoblastoma in 20 million births, these three types of blindness all being dominant. The present annual incidence of blindness is about 12,500 cases in England and Wales. The British report further concludes that probably the total effects of doubling the mutation rates would be slight in the first generation for neonatal deaths, stillbirths, and congenital malformations. This prediction is one which would be modified considerably had the British committee taken the point of view adopted by the American group, namely, that there is a very considerable risk of heterozygous damage, amounting possibly to a 10 percent increase in the first generation, after a doubling of the mutation rate.

In the case of traits influenced by heredity which show a continuous normal frequency distribution, such as stature, general health, life span, intelligence, and the like, the British report points out that in any single generation the fraction of the total variation due to fresh mutation is very small. Hence "a doubling of the mutation rate for a few generations would be expected to have only the most trivial effect on the variation in such characters, and even a persisting doubling of the mutation rate would take very many generations to approach its full effect, which at most would be to double the variation." A change of the latter sort would, if the distribution is symmetrical, in the long run nearly triple the number of persons falling short of an I.Q. of 70 and consequently requiring special schooling; but also a tripling of the number of persons exceeding an I.Q. of 130. If, however, the distribution is not symmetrical, then the effect by and large is to increase disproportionately the extreme opposite to that toward which natural selection has been pushing the population. Hence if there has been selection in the human species for higher intelligence and if the distribution is not symmetrical, a doubling of the mutation rate would lead to a relatively greater increase in the proportion of those with low intelligence.

The third method used by the American committee to estimate the genetic damage done by radiation consists simply of calculating the total number of mutant genes that would be produced and passed on to the next generation after a given dose to the population. Using 10 r as the dose to the gonads, several geneticists, by two independent methods, have arrived at estimates that cluster fairly closely around an average of 5,000,000 mutations in 100 million children, with an uncertainty of one order of magnitude on either side of the average. To translate such values into the amount of harm done involves so much further uncertainty that it was not attempted.

The British report points to three direct studies of the children of persons who were exposed to ionizing radiations. Two, on the children of American radiologists, are rated as inconclusive; the third, that conducted by the Atomic Bomb Casualty Commission on the children of exposed survivors of the Hiroshima and Nagasaki explosions, was necessarily limited as yet to the first generation of descendants, and is very difficult to interpret. The British committee holds that the data point to a slight but significant change in the sex ratio at birth which might be due to genetic damage, and adds that a doubling in the incidence of congenital malformations or a 50 percent rise in the frequency of stillbirths might have escaped detection even if in fact occurring. Against this interpretation must be placed the silence of the American committee, which included J. V. Neel, the director of the ABCC study. That silence implies a lack of significant conclusions from the Nagasaki-Hiroshima data at the present time.

The American committee has made six specific recommendations. The tenor of the conclusions of the British committee adds great weight to these specific recommendations, which are as follows:

(A) That, in view of the fact that total accumulated dose is the genetically important

figure, steps be taken to institute a national system of radiation exposure record-keeping, under which there would be maintained for every individual a complete history of his total record of exposure to X-rays, and to all other gamma radiation. This will impose minor burdens on all individuals of our society, but it will, as a compensation, be a real protection to them. We are conscious of the fact that this recommendation will not be simple to put into effect.

The British report recommends the keeping of such records for all persons exposed occupationally to radiations, but does not apply the recommendation to the general population.

(B) That the medical authorities of this country initiate a vigorous movement to reduce the radiation exposure from X-rays to the lowest limit consistent with medical necessity; and in particular that they take steps to assure that proper safeguards always be taken to minimize the radiation dose to the reproductive cells.

The British report likewise calls for adequate justification of all employment of ionizing radiations, however small; for close inspection of all sources of radiation, both medical and industrial; for safety instruction of those who use radiations; for a review of the present practice in medical diagnostic radiology; for critical examination of the uses of radiotherapy in nonmalignant conditions; and for the reduction of irradiation as much as possible from miscellaneour sources, such as shoe-fitting, X-ray machines, luminous watches and clocks, and television apparatus.

(C) That for the present it be accepted as a uniform national standard that X-ray installations (medical and nonmedical), power installations, disposal of radioactive wastes, and all other humanly controllable sources of radiations be so restricted that members of our general population shall not receive from such sources an average of more than 10 roentgens, in addition to background, of ionizing radiation as a total accumulated dose to the reproductive cells from conception to age 30.

The British report does not recommend a specific dose level for the population, but states that one must be set, that it is not likely to be more than twice the dose already received from the natural background, and that it might be appreciably lower. The level recommended as a maximum by the American committee is therefore somewhat *higher* than the permissible level anticipated by the British.

(D) The previous recommendation should be reconsidered periodically with the view to keeping the reproductive cell dose at the lowest practicable leevl. If it is feasible to reduce medical exposures, industrial exposures, or both, then the total should be reduced accordingly.

The British committee's point of view is clearly in accord.

(E) That individual persons not receive more than a total accumulated dose to the reproductive cells of 50 roentgens up to age 30 years (by which age, on the average, over half of the children will have been born), and not more than 50 roentgens additional up to age 40 (by which time about nine-tenths of their children will have been born).

The British report recommends a continuation of the present permissible weekly level for occupationally exposed persons of not more than 0.3 r weekly, for not more than 13 consecutive weeks. It adds that no person should receive a total of more than 200 r of whole-body radiation, in addition to the natural background, and spread over tens of years; and that no one should accumulate a total dose to the gonads of more than 50 r from conception to age 30. The last allowance should not apply to more than one-fiftieth of the total population. It is obvious that the 100 r allowance per person by age 40, as recommended by the American committee, and the 200 r lifetime allowance, recommended by the British committee, are practically equivalent.

(F) That every effort be made to assign to tasks involving higher radiation exposures individuals who, for age or other reasons, are unlikely thereafter to have additional offspring. Again it is recognized that such a procedure will introduce complications and difficulties, but this committee is convinced that society should begin to modify its procedures to meet inevitable new conditions.

This proposal was not paralleled by the British.

As to final conclusions on this subject, both reports emphasize that the present and foreseeable hazards from fall-out resulting from the test explosions of nuclear weapons, fired at the present rate and proportion of different kinds, are negligible; but the British stress also that account must be taken of the *internal*

radiation from radio-active strontium accumulating in bone.

Both reports also stress the great existing gaps in our present knowledge of human genetics, and urge that much effort be expended to fill them. The American report calls for fundamental research in all branches of genetics, and especially human radiation genetics. The British report calls for further data on the genetic structure of human populations, by means of a greatly expanded collection and analysis of vital statistics. The American report says: "The present state of advance in atomic and nuclear physics on the one hand, and [that] in genetics on the other hand, are seriously out of balance . . . Our society should take prompt steps to see to it that the support of research in genetics is substantially expanded and that it is stabilized." It seems clear that the British committee implicitly, if not explicitly, urges the same.

Few more fateful documents have been submitted to the consideration of the modern world than these two reports. They in no way claim finality. Yet what they say is of such urgency and such far-reaching significance that every tool of public education and legislative power needs to be fully employed in promoting a wider appreciation of the foreseeable hazards, not alone of a nuclear war, but equally of the expansion of peaceful uses of atomic energy. It is shocking to realize that already virtually half of the maximum reasonable allowance of exposure for the whole population is preempted by medical and dental diagnostic and therapeutic uses of ionizing radiation. We must henceforth guard jealously every expenditure of this radiation allowance. The cost of negligence would be genetic bankruptcy, and from that bankruptcy there might be no recovery, for nation or for mankind.

ASYNAPSIS AND PLASMODIAL MICROSPOROCYTES IN MAIZE FOLLOWING X-IRRADIATION OF THE POLLEN

D. T. Morgan, Jr.*

MAJOR changes in chromosome structure induced by X-irradiation of maize pollen result in departures from the usual synaptic configurations during meiosis in the next generation. Ordinarily, the altered pairing is a direct and explicable result of a specific type of aberration with the change in relationships confined to the rearranged chromosome from the irradiated sperm and the normally arranged homologue derived from the untreated egg cell. Recently, indirect and rather unusual meiotic effects involving all chromosomes of the complement were observed in connection with the deficiency of a chromosome in a set of X-ray induced twins of *Zea mays*. Failure of normal first division association of homologous chromosomes was observed in both members of the set of twins. Also, the asynaptic microsporocytes were frequently fused into large plasmodial masses, presumably due to premeiotic suppression of cytokinesis.

The asynaptic twins occurred as a part of a larger study on X-ray induced polyembryony in maize. In addition to the well-known induction of chromosomal aberrations, X-irradiation of the pollen frequently has a significant effect on subsequent embryonic development. In comparison to control populations, the frequencies of twin, triplet and quadruplet seedlings are greatly increased in the F_1 following X-irradiation of the pollen[10]. Cytological studies of such multiple seedlings of maize and data from genetically marked crosses show that deficiencies induced in the sperms may result in cleavage during embryogeny, thus leading to the formation of identical multiple embryos[9]. The present study is an account of meiotic observations in one set of X-ray induced twins.

Materials and Methods

Pollen of inbred line CI3A was irradiated at a target distance of 30 cm. with 1000 r units of X-rays delivered at the rate of 23 r per minute from a General Electric Maximar 100 unit. The unit was operated at 100 kvp. and 5 ma. with 3 mm. of aluminum added filtration. Plants of inbred line CI3A were crossed with the irradiated pollen. The resulting kernels were placed in a germination chamber, and the set of twins reported in this paper was isolated from the seedling population.

Microsporocytes and root-tips of the twins were fixed in three parts of 95 percent ethyl alcohol and one part of glacial acetic acid. The twins were phenotypically normal during growth, but both members were entirely sterile at maturity. The anthers were not exserted and no kernels were obtained following crosses with pollen from inbred line CI3A. Aceto-carmine smears of microsporocytes and root-tips were prepared from previously collected material after the sterile nature of the twins was detected. Also, root-tips were fixed in Randolph's modification of Navashin's fluid; paraffin sections were cut at 14 microns and stained with crystal-violet.

Cytological Observations

Cells with 19 chromosomes and a fragment and cells with 19 chromosomes were observed in both aceto-carmine smears and crystal-violet sections of root-tips from the two plants.

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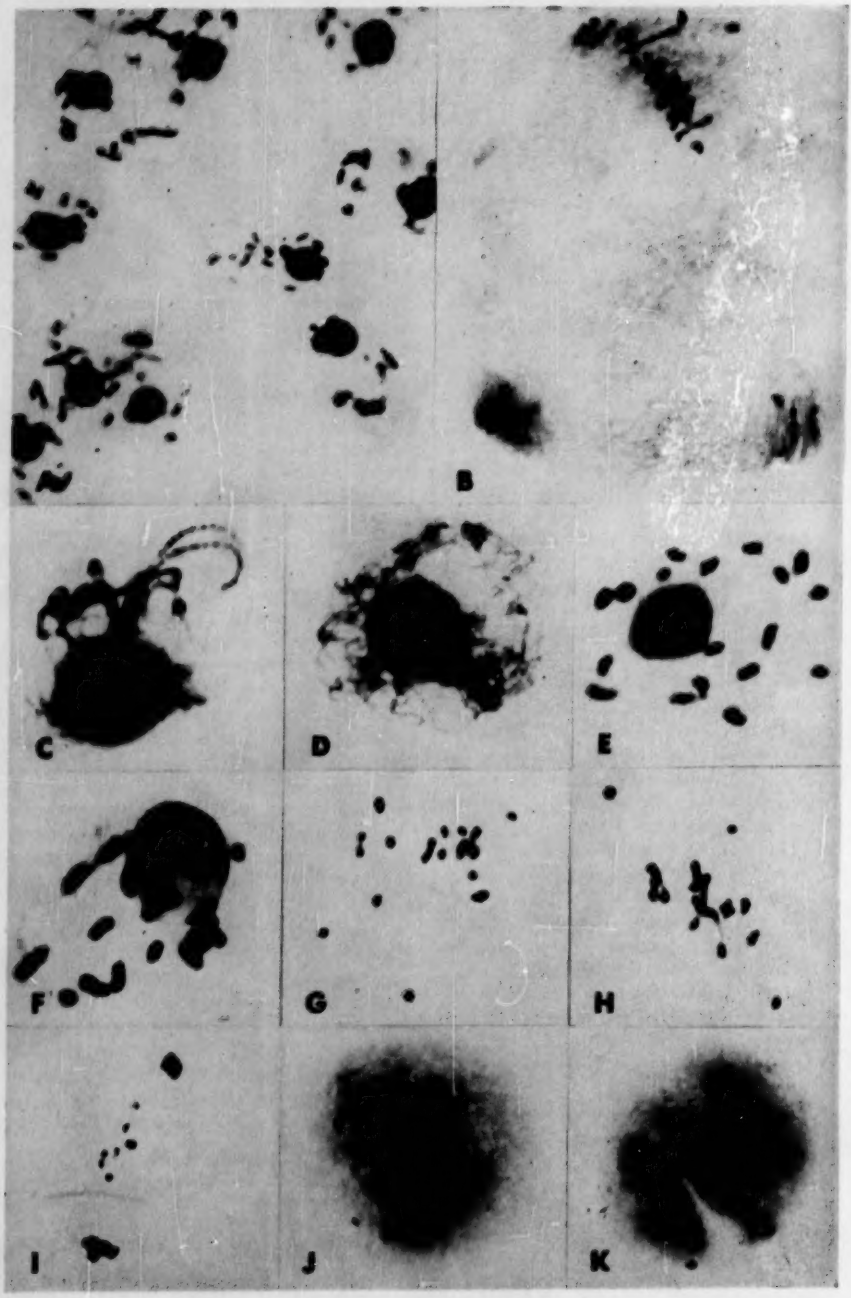
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Except for the fragment and its loss from some cells, no deviation from normal mitosis was evident. Since the same chromosome numbers were observed in both of the twin plants, it seems apparent that the twins were monozygotic in origin and arose by cleavage during an early phase of embryonic development. In addition to the genetic identity of the twins, environmental conditions were similar, since the two members grew adjacent to each other. Consequently, a distinction between the asynaptic twin plants will not be made in the following account of meiosis.

In the majority of the anthers, the pollen mother cells occurred in large plasmodial masses, presumably because of premeiotic suppression of cytokinesis. Individual microsporocytes were present in other anthers. The plasmodial masses, containing numerous asynaptic nuclei, were disrupted during the preparation of acetocarmine smears. A portion of a plasmodial mass with 10 asynaptic nuclei at diakinesis is shown in Figure 4*A*. Hyperploid and hypoploid chromosome numbers occurred at metaphase I in the plasmodial masses (Figure 4*B*). The hyperploid metaphase configurations were crowded and difficult to count. Hypoploid first metaphases consisting of a single bivalent or a few bivalents and univalents occurred along with hyperploid configurations in the same plasmodial mass. Since the nuclei were frequently in close proximity in the plasmodium (Figure 4*A*), it seems likely that some of the chromosomes from originally separate nuclei entered into the formation of a common metaphase plate, thus accounting for the formation of metaphase configurations with more and with less than the expected number of chromosomes.

First division stages were studied in microsporocytes from anthers where plasmodial formation had not occurred in order to obtain a comparison with asynapsis in maize due to the recessive gene *as* described previously by Beadle[1,8]. Prepachytene stages in maize are not susceptible to detailed analysis. At zygotene in normal material, the chromatin threads are closely appressed against the nucleolus with an occasional synapsed free arm extending from the knot of chromatin[15]. The free arms extending from the synizetic knot were well paired in all of the 31 pollen mother cells of the asynaptic twins examined at this stage (Figure 4*C*). Some microsporocytes exhibited an apparently later stage in which the chromatin was not drawn closely against the nucleolus and the strands were not paired (Figure 4*D*). This stage was interpreted as a desynapsed pachytene rather than a prepachytene stage since the chromatin strands were not appressed against the nucleolus and appeared more condensed than those characteristic of the earliest prophases of maize. Individual chromosomes could not be identified in the tangled and largely unpaired pachytene figures.

Although diplotene preparations were obtained, they were not abundant or satisfactory for analysis. The 49 cells studied at diakinesis ranged from complete asynapsis with 19 univalents to a maximum association of eight bivalents and three univalents. The two homologous chromosomes of a bivalent were associated in an end-to-end arrangement (Figure 4*F*), unlike the side-by-side arrangement of pseudobivalents at diakinesis observed in the F_1 generation of *Secale montanum* following X-irradiation of the pollen[12]. A single ring bivalent was observed in each of three cells; the other bivalents were terminally associated rods. Similarly, Beadle[8] reported that most of the chiasmata were terminal at diakinesis in asynaptic homozygotes of maize. The fragment chromosome detected in some of the root-tip cells was apparently lost prior to meiosis since it was not observed at diakinesis or metaphase I.

At metaphase I the spindle and the arrangement of the chromosomes appeared similar to that described by Beadle[8] for asynaptic homozygotes. The univalents were widely distributed while the bivalents were generally located near the center of the curved, elongated spindle (Figure 5). With a few exceptions, the bivalents were rod-shaped with the homologues associated by a tenuous terminal connection (Figure 4*G*). As pointed out by Soost[19], determinations of associations in asynaptic material at metaphase I are subject to considerable inherent error since all of the bivalents do not disjoin simultaneously at the inception of anaphase I. Dyads derived from the precocious disjunction of some bivalents are thus easily confused with univalents. Attempts to score metaphase I configurations before any disjunction is initiated result in the exclusion of those cells with few associations, since univalents in close

X-RAY INDUCED ASYNAPSIS

Figure 4

←— *A*—Plasmodial mass of microsporocytes at diakinesis. Note the close proximity of the configurations at the lower left. *B*—Plasmodial metaphase I with hyperploid and hypoploid configurations. *C* through *K* are photomicrographs of individual cells. *C*—Late zygotene or early pachytene with synapsed free arms extending from the knot of chromatin around the nucleolus. *D*—Later pachytene with unpaired chromosomes. *E* and *F*—Asynaptic diakinesis showing univalents and terminally associated bivalents. *G* and *H*—Univalents and bivalents at metaphase I. *I*—Telophase I with lagging, dividing univalents. *J*—Telophase I showing division of a univalent. *K*—Interkinensis with micronuclei and irregular cytokinesis. The approximate magnifications are: *A*, *I*, *J*, *K*—550×; *B*, *G*, *H*—700×; *D*, *E*—1000×; *C*, *F*—1200×.

ASYNAPTIC MICROSPOROCYTE AT METAPHASE—ANAPHASE I

Figure 5

Note the elongated spindle and the widespread distribution of univalents. Approximate magnification, 750×.

proximity may falsely appear to be the result of anaphase separation of bivalents. A detailed analysis of each of the 86 metaphase I configurations studied will not be given because of the tenuous nature of the associations and the inherent errors in the scoring of asynaptic metaphase I cells. However, a range in configurations from eight bivalents and three univalents to no detectable associations was observed. Cells having three or four bivalents occurred most frequently.

As observed by Beadle[9], metaphase I and anaphase I are usually not sharply differentiated in highly asynaptic material due to the widespread distribution of univalents along the elongated spindle. However, some well defined telophase I cells were observed in the twins. Telophase I (Figure 4*I*) was characterized by varying numbers of laggards, and the division of univalents was observed in some microsporocytes (Figure 4*J*). Micronuclei were frequent in the highly irregular interkinetic cells (Figure 4*K*). Infrequently, an interkinetic cell was observed containing a single restitution nucleus. Second division stages were not found in the material from the twin plants.

Discussion

The plasmodial microsporocytes and asynapsis observed in the maize twins in part simulate meiotic effects conditioned by recessive genes. Plasmodial groups of microsporocytes, accompanied by various deviations in chromosome number, size and association, have been attributed to the action of two different recessive genes in barley[6,18]. In maize, Beadle[9] observed plasmodial masses of microsporocytes in some plants of cultures homozygous for the recessive gene, *variable sterile*. However, the reports most pertinent to the meiotic analysis of the X-ray induced twins are those of Beadle[1,8] on genetically controlled asynapsis in maize. The first meiotic division in individual microsporocytes of the X-ray induced maize twins closely paralleled that described by Beadle for asynaptic homozygotes. Beadle concluded that there was a tendency toward the failure of chiasmata formation following synapsis, resulting in the disassociation of homologues. Consequently, decreases occurred in the number of chiasmata per bivalent and in the number of bivalents per cell at diplotene, diakinesis and metaphase I. Rhoades[14] and Rhoades and Dempsey[16] found significant increases in the frequencies of crossing-over for the two marked regions tested in chromosomes 2 and 9 in asynaptic homozygotes of maize. The genetical data thus substantiate Beadle's cytological observation that synapsis does occur in asynaptic maize. A reexamination of permanent slides prepared by the author in 1948 from asynaptic homozygotes suggests that asynapsis and a premeiotic suppression of cytokinesis may be partially related. Infrequently, the union of two microsporocytes is observed in otherwise normal material. However, the fusion of two or more cells at pachytene and diakinesis was detected in seven of 12 permanent slides of microsporocytes from asynaptic homozygotes.

The term asynapsis has been used in the literature to denote failure of expected association of homologues during the first meiotic division. In the frequent instances where observations have been confined to diakinesis or metaphase I, it has been impossible to determine if the lack of association was the result of an initial absence of synapsis or a subsequent disassociation of homologues following zygotene pairing. Li, *et al.*[7] designate the latter condition as desynapsis in contrast to asynapsis or the initial failure of synapsis. Previous reports of a lack of association at diakinesis following X-irradiation are mainly limited parts of larger studies or do not include observations on the critical early prophase I stages[5,17]. In so far as it was possible to determine from observations of the free arms extending from the synizetic knot, initial pairing of homologues occurred in the microsporocytes of the twins similar to that reported by

Beadle[5] for genetically controlled asynapsis in maize. Although the term desynapsis seems more appropriate for the present study and the previous one by Beadle, it seems advisable to continue the use of the older and more general term, asynapsis, in order to avoid confusion, since the meiotic observations of the two studies are essentially similar.

The extensive earlier literature pertaining to asynapsis in various species of plants, its causes and its bearing on theories of meiosis has been summarized by Prakken[12] and discussed more recently by Soost[19] and Celarier[4]. Consequently, a recapitulation of these topics will not be presented here. However, a study by Huskins and Hearne[6] is pertinent in that it attributes asynapsis to the loss of a specific chromosome pair in dwarf fatuoid oats and dwarf speltoid wheat. Recently, Person[13] observed limited or partial asynapsis in monosomics for 10 different chromosomes of wheat. Partial asynapsis was detected in every monosomic plant studied. Although the expected associations of 20 bivalents and one univalent were in the majority, cells with as many as 9 univalents occurred with limited frequency. Asynapsis was much more pronounced in the twin seedlings of maize, since the maximum possible bivalent association was not observed at diakinesis or metaphase I. Nevertheless, Person's meiotic analysis of monosomics in wheat is pertinent in regard to attributing asynapsis in the maize twins to the loss of a specific chromosome. Although undetected X-ray induced changes may have occurred, it seems likely that asynapsis and the formation of plasmodial microsporocytes were correlated with the loss of a chromosome in the twin plants of maize. The meiotic abnormalities may thus have been the result of altered dosage relationships of specific genes governing the regular meiotic processes or a reflection of more generalized physiological disturbances in the deficient cells. The recessive gene *asynaptic* is located on chromosome 1 in maize. Although the twins received a normal chromosome 1 from the female parent, it is tempting to speculate that the asynaptic effect was due to the loss during development of the X-rayed chromosome 1 from the male parent. The fact that monosomics for 10 different chromosomes of wheat exhibited partial asynapsis makes such an interpretation dubious.

Summary

Pollen of the maize inbred CI3A was exposed to 1000 r units of X-rays. Sib plants of CI3A were crossed with the irradiated pollen. The set of twin seedlings reported in this paper was isolated following germination of the resulting kernels.

Cells with 19 chromosomes and a fragment and cells with 19 chromosomes were observed in the root-tips of both monozygotic twin plants.

The pollen mother cells of the twins were asynaptic. In the majority of the anthers, the microsporocytes occurred in large plasmodial masses, presumably due to a premeiotic suppression of cytokinesis. Hyperploid and hypoploid metaphase I configurations were observed in the plasmodial microsporocytes. The close proximity of nuclei in the plasmodial masses suggested that some of the chromosomes from originally separate nuclei entered into a common first metaphase group, thus accounting for the formation of metaphase configurations with more and with less than the expected number of chromosomes.

Individual microsporocytes from anthers where plasmodial formation had not occurred were studied in order to obtain a comparison with asynapsis in plants of maize homozygous for the recessive asynaptic gene. As reported by Beadle for asynaptic homozygotes, synapsis occurred in microsporocytes of the twins, as evidenced by the paired nature of the free arms extending from the synizetic knot. The chromosomes in later pachytene stages were largely unpaired. The fragment chromosome, presumably lost in premeiotic divisions, was not detected in the pollen mother cells of the twins. The tangled nature of the largely unpaired pachytene chromosomes did not permit identification of the missing chromosome.

Configurations ranging from 19 univalents to eight bivalents and three univalents were observed at diakinesis and metaphase I. The bivalents were, with few exceptions, in the form of rods.

Laggards were frequent at telophase I, and the division of univalents was observed in some microsporocytes. Micronuclei occurred in the highly irregular interkinetic cells. Second division stages were not obtained in the meiotic material from the twin plants.

Both members of the set of twins were entirely sterile.

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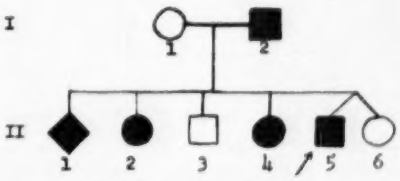
HEREDITARY ABSENCE OF RADIUS AND THUMB

A Report of an Additional Family

EDWARD O. DODSON*

ABSENCE of the radius is a well-known, although fairly rare, defect. Kato[6] reviewed the subject comprehensively, and found a total of 253 cases, including the three new cases with which his study began. Each of his cases represented the only known occurrence in the family, and he discounted the possibility of a hereditary etiology. He notes, however, that previous authors have found cases of familial occurrence of this defect. Thus Bouvier[4] described a family in which the father and four of his five children were affected with absence of the radius and club hand. Blencke[3] described a family in which the first, second, seventh, and ninth children were similarly afflicted. Joachimsthal[5] studied a family in which the mother and five children showed this anomaly. Curiously, he also discounted the role of heredity, attributing the defect to the influecne of amniotic abnormalities.

Birch-Jensen[2] has published an extensive review of congenital deformities of the arm, including 73 cases of absence of the radius. He found the incidence in the Danish population to be about 1 in 55,000. However, as the death rate among the patients is very high in the first two decades of life, he believes that the incidence at birth is nearer 1 in 30,000. As regards inheritance, Birch-Jensen found that most of his pedigrees indicate dominance but a very few pedigrees suggest a recessive gene. Over half of his cases were sporadic, and he considers them to be of nongenetic origin. However, his sporadic cases and presumed recessive cases could be understood on the basis of dominant mutation in one of the parents. His 73 propositi include two twins, both fraternal, and both discordant with their co-twins with respect to the radial defect.



PEDIGREE FOR ABSENCE OF THUMB AND RADIUS

Figure 6

The defect is bilateral and involves both thumb and radius in I-2 and II-5 (the propositus); it is unilateral in II-1 and II2; and it involves only the left thumb in II-4 .

Discussion

The propositus in the present study was a six-week-old boy who was admitted to the Northern Indiana Childrens' Hospital for a gastro-intestinal disorder. This responded to treatment satisfactorily, however, it was observed that both thumbs were missing, and that the hands rested at right angles to the forearm, being displaced toward the radial side. Radiograms confirmed the complete absence of the thumbs and radii. The child was unable to abduct the thighs effectively, and so congenital dislocation of the hips was suspected but not proven. The boy was one of a pair of twins of unlike sex, his sister being normal.

Both parents are living and were available for interview. The mother is normal, but the father (I-2 on the pedigree, Figure 6) also shows bilateral absence of radius and thumb. They have a total of six children. The first (II-1) showed the same deformity unilaterally, and died of broncho-pneumonia at three months of age. The second child (II-2) a girl, has a similar deformity of the left arm, however, it has been fairly successfully corrected by orthopedic surgery. The third child (II-3) is a normal boy. The fourth (II-4), a girl, has a deformed left thumb, but is otherwise normal. II-5 and II-6 are the propositus and his normal twin sister.

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Further data on this family would be most desirable, but could not be obtained because of the uncooperative character of the parents. They were highly chary of genetic investigation. It is particularly unfortunate that their permission could not be obtained to publish the radiograms, however these are similar to figures 54, 55, and 56 of Birch-Jensen[2]. The father indicated that his was the first case among his relatives. Whether or not this is true, the pedigree conforms well to the expected pattern for a trait determined by a single, autosomal, dominant gene with complete penetrance. The expressivity of this gene appears to vary considerably, for the defect is bilateral and involves both thumb and radius in I-2 and II-5; it is unilateral in II-1 and II-2; and it involves only the left thumb in II-4. While it is possible that the last is an independent effect, based upon a different gene or upon a non-genetic factor, it seems more probably that this represents a minimal expression of the same gene. Unfortunately, no radiogram is available to determine whether I-4 has any subclinical abnormality of the radius. Birch-Jensen also noted the wide range of expression of this gene.

The propositus in the present study died at six months of age, and an older sib (II-1), also affected, had died at three months of age. Birch-Jensen[2] also found a high mortality in cases of congenital radial defect, as evidenced by the age distribution of the propositi, over 60 percent of them being twenty or younger. He explained this on the basis of increased incidence of other defects, especially congenital heart disease.

Birch-Jensen[2] treats his sporadic cases as though they were non-genetic in etiology. While this may be correct, comparison to other disorders such as hemophilia[1], achondroplasia[7], and retinoblastoma[8] suggests the possibility that each sporadic case may represent a mutation in one of the parents. So extensive a study as that of Birch-Jensen might have provided good data for estimation of the mutation rate of the gene, had the data been collected with that in mind. He believes that, because of the complete cooperation of Danish hospitals and physicians, he studied every victim of deficient radius living in Denmark during the years of his study, 1943—1947. But he did not get any still births or short lived babies, thus biasing this data by the elimination of the most severely defective cases.

An attempt is here made to use the data of Birch-Jensen in order to make a rough estimate of the rate of mutation of the gene under study. He does not state the date of birth of most of his propositi, however, for purposes of calculation the assumption is here made that the 12 sporadic propositi who were stated to be four years old or younger at the time of examination were born during the period of the study. This assumption certainly is not correct for all of them, but probably is correct for most of them. The bias so introduced is partly, and probably even excessively, compensated by the fact that affected children were missed if they were still born or very short lived. According to the United Nations Demographic Yearbook[9], the total number of births in Denmark from 1943 through 1947 was 457,874. Thus twelve new mutants correspond to a mutation rate of 1.3 per 100,000 gametes, well within the ordinary range of human mutation rates. Some of the twelve cases may be phenocopies or normal overlaps and would cause an overestimation of the mutation rate. This should be compensated to an undeterminable degree by the failure to record cases among still births and short lived children.

Summary

A pedigree of congenital absence of radius and thumb is presented. This is explained on the basis of a dominant gene with highly variable expression. The mutation rate is tentatively estimated at 1.3 per 100,000 gametes.

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A NEW "LUXOID" MUTANT IN MICE

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SINCE Rabaud's first announcement of the congenital absence of the tibia in mice,[10] several like or similar conditions in mice of certain other strains have been reported. Hovelacque (1920-23) and Rabaud and Hovelacque (1923) studied the anatomy of this mutation in great detail. Margaret Green and her co-workers[7] have described a similar abnormality which, like Rabaud's, is associated with polydactylism. T. C. Carter[1] has done considerable work on an abnormality which he calls luxate. Carter's abnormality also involves polydactylism.

A few years ago a stock of polydactylous mice was developed by the senior author of this paper. The origin of polydactylous and a derived "luxoid" stock will be discussed more in detail elsewhere in this paper. Suffice it to say that polydactylia arose in a mouse of the Brpb subline of the NHO mice. These mice (the NHO) had been treated years previously for 22 generations with methylcholanthrene.[19-11] After polydactylia arose in this methylcholanthrene-treated descent no further treatment with methylcholanthrene was used. Later brachydactylous mice[6] and the present condition, the luxoid syndrome, also arose from this same Brpb ancestry.

Material and Methods

All mice used in this study were derived from a single descent of mice as described in the section "The Origin of the Luxoid Mouse." The polydactylous breeders which produced all luxoid mice were continued by brother to sister matings. When a litter was born the young were classified as to whether they were polydactylous on both hind feet, polydactylous on either left hind or right foot, polydactylous on three or four feet, luxoid or normals. By the use of a magnifying glass, it is possible to make all these classifications with very little chance of error at birth. Even those which are partially mutilated by their mothers can usually be diagnosed. The luxoids can be easily recognized by the following criteria: luxation of all limbs, open eyelid, hydrocephalic doming of the skull, alopecia and a paleness in skin color associated with mild anemia. In addition to these variations polydactylism and luxations are always present on all four feet.

Many of the luxoid females and males were tested for sterility. Luxoid mice were mated to luxoids. Both parents possessed all the characters of the complete syndrome. Many female luxoids (complete syndrome) were mated to non-luxoid polydactylous males; several luxoid males were mated to non-luxoid polydactylous females. When the first special (designating an incomplete presence of the complete luxoid syndrome) female luxoid appeared she was mated to a non-luxoid polydactylous male.

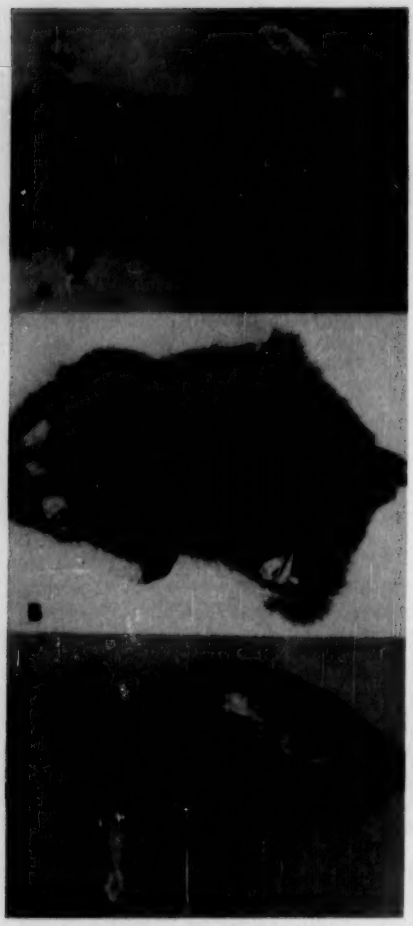
The anatomical studies were made on gross appearance, dissection, staining techniques,[4] X-ray photography and ordinary photography (see Figures 7-9).

The mice in the Springville laboratory are housed in wooden boxes which are cleaned once a week. The colony room is light and airy and it is kept at about 70-80 degrees F. Air conditioning is not used. The mice are fed a diet of Nurishmix. This standard pelleted food is supplemented by a mixed grain diet which has a small amount of cod-liver oil. Further details of this feeding regime have been published[20]. Water is given *ad libitum*.

Origin of the Luxoid Mouse

Briefly stated, the origin of the "luxoid" mouse was as follows. Mice of the

*Biological Station of Roswell Park Memorial Institute, Springville, New York. The authors are indebted to Mr. Charles Herger, X-ray technician and Mr. William Payne, Medical photographer, of Roswell Park Memorial Institute for preparation of the illustrative material.



A MALE LUXOID MOUSE

Figure 7

A—A ventral view showing the torsion of the right leg. The leg is twisted under the animal instead of up against the lateral and dorsal surface. *B*—A dorsal view showing, in addition to the luxation of the legs, the hydrocephalic doming of the skull and the lack of hair (alopecia) on the head. *C*—A lateral view showing the bending of the hind leg.

CBA and N strains were crossed. After nine generations of sib-matings, a male (F_9 128127) was outcrossed to a female (F_{20} 128150) of the JK inbred strain. In the F_4 following this outcross, the mice were divided into four groups. Of these four groups, three were maintained as controls by brother-sister matings. The mice of the fourth group were injected subcutaneously at 60 days of age with 1 mg. of methylcholanthrene dissolved in 1 cc. of sesame oil and continued by sib-matings as breeders. This descent constitutes the NHO subline (descendants of F_4 143960 male and F_4 143962 female). The NHO were then separated, during the summer of 1943, into four further sublines, the pBr, Br, Brpb and pBrpb. The F_{18} 259103 (Brpb subline) female mouse was continued and her descendant F_{25} 308328 female was the mother from which F_{26} 317251 was obtained. This male mouse showed the first case of polydactylia (on right hind foot). From this point on no more mice of this descent received methylcholanthrene. This male (F_{26} 317251) was then outcrossed to F_{29} 326622 female of the C_{57} strain. In the F_4, a polydactylous mouse (F_4 355275 male) with a triple left hallux and a polydactylous right (both on the hind feet) was mated to a female (F_4 355270) which had polydactylia on both hind feet. From this mating eventually arose the first luxoid (mouse No. F_5 362938) sex undetermined; see Table I for the pedigree of the first luxoid mouse).

Results

In a total of 1,777 mice in this one restricted descent of polydactylia by polydactylia there were (1) 485 mice with all four feet normal; (2) 1,040 polydactylous mice as indicated in

TABLE I. Origin of the Springville luxoid mouse. This is a somewhat schematic pedigree (condensed) of the origin of the Springville luxoid mouse. Polydactylous male (F_{26} 317251) was obtained from a descent of mice of several generations which had been treated at 60 days of age with methylcholanthrene for a period of twelve years. This male was then outcrossed to C_{57} female (F_{29} 326622) and the young of this mating were sib mated. In the F_4 of the sib matings the first luxoid mouse (F_5 362938) appeared.

♀		♂
F_{29} 326622 C_{57}	×	F_{26} 317251 Poly
F_1 338332	×	F_1 338333
F_2 345419 Poly left	×	F_2 345360 Poly both
F_3 349681 Poly both	×	F_3 349391 Poly left
F_4 355270 Poly both	×	F_4 355275 Poly right Triple left

F_5 362938
First Luxoid

the following break-down; (3) 993 were polydactylous on both hind feet; (4) 18 were polydactylous on the left hind foot only; (5) 29 were polydactylous on the right hind foot only; (6) 201 were luxoids showing the complete syndrome and (7) 13 were special luxoids. These special luxoids include all partial luxoids and those containing the complete syndrome plus other defects such as hair lip, umbical hernia and craniorachischisis. (8) 34 mice were found to have polydactylism on three feet without luxoid and (9) 18 were found to have polydactylia on all four feet without being luxoids, (see Table II).

The results of the breeding experiments of luxoids are as follows: For a long time breeding experiments could not be conducted because all luxoid animals died at birth or shortly thereafter suggesting a semi-lethal effect of the luxoid syndrome. However, after a while several female and male luxoids were raised to weaning age. These were tested for fertility or sterility as described previously. When a luxoid female showing a complete syndrome was mated to a luxoid male showing complete syndrome no pregnancies occurred. When a complete luxoid female was mated to a polydactylous non-luxoid male no pregnancies ensued. The same was true when a non-luxoid polydactylous female was mated to a luxoid male. However, when a special (an incomplete expression of the syndrome—all characters being present except one normal eye) luxoid female was mated to a non-luxoid polydactylous male, she became pregnant and produced a litter of all polydactylous young—no luxoids being present. Another special luxoid female (F. 394284) showing luxation on only the left hind foot has produced three litters when mated to a polydactylous (non-luxoid) male (F. 394285). The young were as follows: 5 normals; 1 luxate on all four feet; 6 polydactylia on right hind foot only. In view of the great scarcity of mice with polydactylia on the front feet by mating polydactylia to polydactylia, these nine out of 16 exceptional front footed polydactylia cases must be highly significant.

The results of the anatomical studies are enumerated below.

Description

In this section a detailed analysis of the Rabaud, Carter, Green and Springville luxoid mice is given and comparisons made between the several mutant types. Anatomical features will be discussed in the following order, wherever practical; (1) the gross external appearance beginning craniad and working caudad; (2) the internal anatomy and (3) the skeletal anatomy, (Table III).

(A) E. Rabaud's Mice

Due to the fact that this strain of mice is extinct, a detailed discussion of the gross appearance of the head is difficult. However Grüneberg[8] has reproduced several plates from Rabaud and we shall base our description on these drawings.

The plates indicate that the conformation of the head is normal. There is no sign of hydrocephaly or alopecia. The eyes appear to be entirely normal. The plates indicate no malformation of the fore-legs. In fact, Grüneberg states: "The skeleton of the fore limbs is entirely normal, except that two out of 242 abnormal animals dissected by Hovelacque showed bilateral polydactylism (six toes)[8]. The dorsum also does not exhibit any tendency toward alopecia.

The abnormality of these luxoid mice of Rabaud lies completely in the hind legs. Polydactylism is usualy present on both hind feet. The tibia is more or less absent. However, even in the most severe cases, a small nodule or spicule of bone representing the tibia can be detected. As a result of this tibial absence the animal attempts to support its weight on the fibula. However, due to the thinness of the fibular bone, and due also to incomplete knee articulations, the weight of the animal cannot be thus supported and the fibula bends even though it does become thicker and stronger than in normal mice. Because of the torsions of the shaft of the fibula, the feet assume an abnormal position to the extent that the plantar surface is at right angles to the axis of the body. Due to this apparent luxation ("souris luxees") of the hind limbs, the animals drag themselves along on their bellies and on the distal end of the femur. This also causes the

TABLE II. The records obtained from the descent of male mouse 355275 mated to female 355270. The distribution of data on polydactylia and luxoid mice are included.

Litter	Total	Normal	Poly	Poly both	Poly left	Poly right	Luxoid	Special luxoid	Poly three	Poly four
1	467	121	258	245	8	5	68	2	13	5
2	346	89	206	200	1	5	17	3	9	2
3	279	72	165	158	1	6	36	1	5	0
4	238	65	117	112	0	5	28	3	5	0
5	168	46	106	101	2	3	11	1	2	0
6	151	49	88	81	3	2	12	2	0	0
7	68	23	44	41	1	2	1	0	0	0
8	41	11	25	22	2	1	5	0	0	0
9	18	4	11	11	0	0	1	1	0	1
10	1	1	0	0	0	0	0	0	0	0
Total	1777	481	1040	993	18	29	201	13	14	8

X-RAY PHOTOGRAPHS OF A LUXOID MUTANT

Figure 8

A—Ventral view. Note the bowing of the foreleg and the absence of the public symphysis. The right foot displays pronounced polydactylia. *B*—Dorsal view. Note the absence of the tibia, the obturator foramen, and the torsion of the hind and foreleg. The patella is shifted slightly to the side. *C*—Lateral view. Of special interest is the torsion of both the fore- and hind leg.

animal to appear to be dorso-ventrally flattened. As a rule, the foot is elongated in the ratio of about 3 : 2 compared to normal feet. Other abnormalities are manifested in the foot. These are (a) fusions between the tarsus and calcaneus, and (b) fusions between the ossa cuneiformia, the os naviculare and occasionally the os cuboidium. In 19 out of 242 cases, polydactylism, exclusive of the big toes occurred. The duplication may be complete or incomplete in varying degrees.

The pelvis and proximal part of the femur are normal. The distal end of the femur is more or less abnormal. The patella is normal although usually laterally displaced.

(B) T. C. Carter's luxate mice

Carter[1, 4] has been able, through breeding experiments, to distinguish between the heterozygote and the homozygote luxate in mice of his stock. (Carter has employed the term luxate since identity with the original Rabaud's luxoid could not be established owing to the loss of Rabaud's colony of mice.)

The external appearance of Carter's mice, except for the feet and hind legs, appears to be normal. There is a tendency of the homozygous luxate to be slightly smaller than its sibs. No hydrocephalic doming of the head was reported and alopecia was not described in even the most extreme cases of luxation. The eyes are apparently normal. All five digits may be three jointed. In the homozygous mouse there are frequently supernumerary elements on the preaxial side of one or both hind feet.

The typical homozygote appears to have a normal thigh. However, the leg below the knee is often twisted. This twisting gives the appearance of a luxation of the hind feet. Here too, the hind feet have their plantar surfaces at right angles to the axis of the body. Of the hind feet of the homozygote both are most usually affected and, as a rule, the right limb is more severely affected. Usually one leg is nonfunctional. This is usually the right one, although occasionally the left. In addition to polydactylism some of the luxates of Carter tend to have a reduction in the number of digits; in some cases there are only three toes.

The internal anatomy of Carter's mice have several highly atypical variations. These include, most dramatically, a condition called "horse-shoe kidney.' In the horse-shoe kidney, the left kidney (posterior pole) approaches the right and in some severe cases becomes fused with the right kidney. Hydronephrosis and hydro-ureter were not uncommon. Ureteric, renal and genital agenesis were also found by Carter in his luxate mice.

The skeletal anatomy of the feet of Carter's heterozygotes show little change from the normal. The homozygotes, on the other hand, show the following variations: the additional digits are accompanied by the additional bony parts; on the other hand, sometimes the foot is reduced from normal leaving only tridactylous feet.

The luxate homozygote also shows decided skeletal defects. The femur is usually shortened. The patella is present but usually shifted laterally. In mild forms of the luxate condition the tibia is merely shortened. In severe cases, the tibia is usually completely absent. When the tibia is absent the fibula is bent due to its unsuccessful attempt to bear the weight of the animal, and, of course, due also to the forces exerted on it by the muscle groups which ordinarily have attachments to the tibia.

Carter's luxate mice tend to have a slight increase in the number of presacral vertebrae. The innominate bones show abnormalities very much like the Springville luxoid.

(C) Margaret Green's luxoid mice

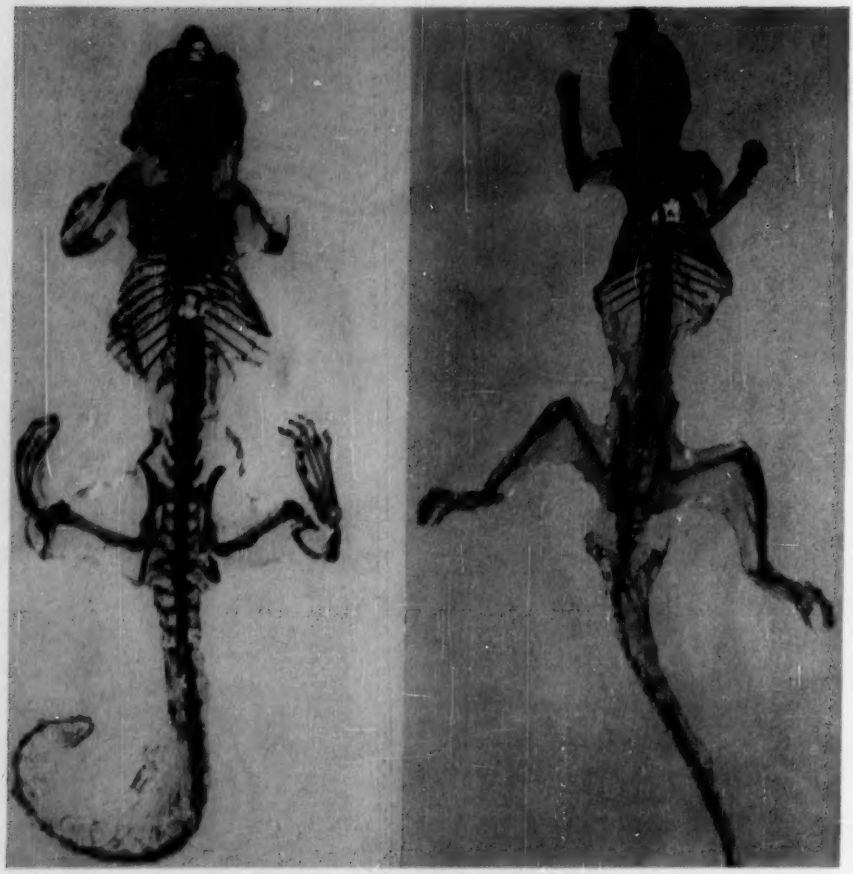
Neither in the plates, nor in the ensuing paper[7] does Margaret Green mention any cranial aberrations. The mouse appears grossly to be normal in all respects excepting the hind feet. The homozygous luxoid tends to have additional sternebrae, ribs and presacral vertebrae.

The forefeet of heterozygotes are entirely normal. The forefeet of the homozygote, on the other hand, may show abnormalities on the preaxial side. Polydactylism appears on the preaxial side. Of 37 homozygotes (both C3H and C57BL backgrounds) reported, seven animals have no forefoot abnormalities[7], two animals have only the right forefeet affected, five animals have only the left affected, and 20 animals have both forefeet affected.

The hind limb defects in Green's luxoid mouse are as follows: (1) occurrence of three instead of two normal bones in the first digit, (2) often a preaxial supernumerary digit is present, (3) "occasionally there is preaxial reduction, the hallux being very much reduced or absent",[7] (4) the tarsal bones usually are abnormal, (5) both feet are always affected, (6) "in homozygous mice the tibia is reduced in varying degrees and the fibula is correspondingly enlarged. . . . In the most common condition the tibia is reduced and the fibula is enlarged to the extent that the two bones are about the same size. Often under these circumstances they are not fused, but form two separate symmetrical bones. In contrast to *lx* (luxate of Carter) which affects predominantly the right side, *lu* (luxoid of Green) in the

TABLE III. A comparison of manifestations of the Springville luxoid syndrome with those of Carter, Green and Rabaud

Character	Springville	Rabaud	Carter	Green
Polydactylia	+	+	+	+
Luxoid (all feet)	+	—	—	—
Luxoid (three feet)	+	—	—	—
Luxoid (both hind feet)	+	+	+	+
Open eyelid (blind)	+	—	—	—
Mild Anemia	+	—	—	—
Hydrocephalous	+	—	—	—
Alopecia	+	—	—	—
Displaced testis	+	—	agenesis	—



LUXOID AND NON-LUXOID POLYDACTYLIA

Figure 9

Left—A dorsal view of a luxoid mouse showing the torsion of the hind leg. Right—A ventral view of a non-luxoid polydactylous mouse. These photographs were taken at about a 1:1 ratio and transmitted light was used. The skeletons were stained by the Alizarin-red technique as devised by Dawson and revised by Hardy.

homozygote is nearly symmetrical in its effect on the two sides. The abnormal tibia causes the knee joint to be very deficient so that the shank and foot are no longer held in normal position".[7] Margaret Green has also found that many of the homozygote mice (*lu lu*) have a tendency toward kinky tail.

(D) The Springville luxoid mice

The most severe type of luxoid mice shall be described first. These are mice which show all of the following deviations from the normal: (1) reduction or absence of the tibia, (2) torsion of the remaining fibula, (3) polydactylia, (4) alopecia, (5) open eyelid, (6) mild anemia, (7) hydrocephaly and (8) semilethal, (Figures 7-9).

The gross appearance is most obvious even in the new born since luxation of all four feet is present. The skull of the anim[illegible] is dome shaped indicating hydrocephaly. A[illegible]pecia is always present on the dorsum, especially on top of the head. The mice exhibit a condition of open eyelid indicating blindness. The forefeet are polydactylous with the supernumerary digits appearing on the preaxial side of the foot. The fore limbs always show luxation. The hindfeet show polydactylous (preaxial)

and severe torsion. This causes the hindfeet to be shifted to a position at right angles to the axis of the body with the plantar surface craniad. The new born also show definite signs of anemia (the severe cases have extreme paleness of the skin and usually die shortly after birth).

The skeletal defects of the fore limb show (1) a shortened humerus, (2) the forearm shows the greatest defect, (3) the ulna is missing and the radius is enlarged and bowed, and (4) in some cases the ulna is still represented as a small bony nodule. However, this vestigial ulna usually has no normal articulations.

The polydactylous condition of the forefeet show true hyperphalangy. The bones of the forefoot (carpals, metacarpals and digits) all show increased size and numbers. The supernumerary digits may not always, in fact they usually do not, show complete bone reduplication. In some cases the extra toes are only rudimentary buds which have growth potentials for the formation of true digits.

There are no marked differences in the number of sternebrae or presacral vertebrae.

The pelvic girdle shows great modifications. The ischium appears to be most severely affected. The rami of the pubis and the inferior ramus of the ischium are missing or greatly reduced. In all cases of mice studied the obturator foramen is completely obliterated (Figure 8). Due to this and other deformities of the innominate bone (the acetabulum) it is not possible for the head of the femur to be properly articulated.

The most striking abnormality of the luxoid mouse is in the hind limbs. The femur is in general slightly shorter than in normal polydactylous mice. The patella is present but in all cases is shifted laterally, due to the lack of patella attachments on the tibia.

In the Springville luxoid mouse the tibia is usually completely lost. In a few cases however, the tibia is represented by a small (1.0 - 1.5 mm) nodule of bone. The fibula, on the other hand, is greatly enlarged and strengthened. The animal has apparently been unsuccessful in compensating for the loss of the tibia, and under the weight of body and the pull of attached muscles (which in the normal animal would be attached to the tibia) the fibula becomes bowed. Figure 8 shows X-ray photographs of the total skeleton of polydactylous and luxoid mice. The foot is always polydactylous when the leg is luxoid.

The extreme form of luxoid always displays a mild anemia which is easily detected at birth. Many of the luxoid which die immediately post partum are believed to be anemic.

The testes of the luxoid males are never carried in the scrotal sac when the luxoid condition is extreme. They cannot be forced into the sac and it is difficult to establish whether or not a scrotum actually exists. The testes usually lie lateral to the midline sometimes within the peritoneal cavity and sometimes between the peritoneum and the integument. In some cases one testis will lie within the peritoneal cavity and the other will lie outside. With the exception of a possible enlarged thymus no other visceral defects were noted in these males.

The female extreme luxoid apparently carries no gross serious visceral or internal defects. The ovaries are normal and during estrus and shortly thereafter ova can be found in the ampulla and in the oviducts. Deviations from the complete luxoid syndrome have, from time to time, appeared in the luxoid mouse at Springville. These are apparently associated, but not strongly so, with the luxoid syndrome. A list of these includes: normal eye, normal blood pictures, normal cranium, hair lip, craniorachischisis and umbilical hernia.

It would be difficult to place these characters on the genetic background due to the inability to perform breeding experiments on this material except in a very few and unusual cases. In some of these cases these variations have appeared only once and this strongly indicates that some of these are due to chance and that they are not really associated genetically with the luxoid syndrome.

Discussion

The luxoid and very similar morphological characters have arisen upon at least four occasions in mice of widely separated colonies; once in France (Rabaud) once in England (Carter), and twice in the United States (Green and Strong). In every case there has been an intimate association with polydactylia and several other variations. The data of Green indicate that perhaps her luxoid character is the ultimate homozygous condition of polydactylia which manifests a complete type of inheritance. However this interpretation does not fit the present data. It has been shown (unpublished data) that by selection of polydactylia × polydactylia over several generations that a very high percentage of polydactylous young can be produced. In one selected subline the penetrance is 92.30 percent of all young born. Many of these females produce young all of which are polydactylous and there is no evidence of luxoid or of any of its associated characters (open eyelid, hydrocephaly, anemia, etc.).

Polydactylia in the front feet is of extremely rare occurrence in the other polydactylous descents genetically related to the single one which produces mice showing luxoid.

The production of special luxoid mice which show only a partial complement of the complete luxoid syndrome is of additional genetic interest. These mice demonstrate that perhaps a complex method of genetic determination is involved in this character. Perhaps with a little selection these components of the luxoid syndrome could be separated.

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✦

GENES AND CULTURE

IN it's author's words this little book* is "an attempt to interpret some of the philosophical implications of modern biology in terms which a layman can understand." In subject matter it is somewhat between H. S. Jennings' "The Biological Basis of Human Nature"† and G. G. Simpson's "The Meaning of Evolution"‡, but briefer and with more about philosophy and ethics.

The present book is an expansion and revision of the author's Page-Barbour lectures at the University of Virginia in 1954. The central theme is man as a social animal and a developer of "cultures." The evolution of cultures is held to operate so differently from biological evolution as to be a qualitatively different kind of process.

Always present, sometimes as a background and sometimes as the focal point of the discussion, is the question of how far the differences between individuals and between races in human behavior are gene-determined and how far they are learned from the immediately surrounding culture, with the genotype merely having to be such that man is capable of learning. As the sentence which seems best to express briefly the author's stand on this, we read on page 29: "An infant is born with a genotype which makes him receptive to conditioning by other human beings with whom he is associated...." The reviewer could endorse this more heartily if the parenthetic expression "(more or less)" were inserted after "receptive." Perhaps the need for brevity forbade that, but some readers might interpret the whole paragraph as a complete endorsement of the more extreme doctrines of John B. Watsonian behaviorism. That such an in-

**The Biological Basis of Human Freedom.* Theodosius Dobzhansky. 139pp. Columbia University Press, New York. $2.95. 1956.

†1930, W. W. Norton and Company.

‡1949, Yale University Press, and 1951 Mentor.

terpretation would not be fair to the author is clear from what he says in many other places. To quote only two such, on page 36 we read: "In bringing about intracultural diversity of personality and behavior, constitutional or genetic variables are most important, ..."; and on page 48 he deprecates such extreme hypotheses as Margaret Mead's words: "We therefore hold human nature constant and assume, for the present, that human nature may be regarded as similar for Bushmen, Hottentots, Americans of 1941, etc."

The need for brevity and for omitting minor qualifications of the main ideas, in order to make those main ideas clear to an audience not well versed in biology, are doubtless the main reasons for occasional near-contradictions in viewpoint or for swinging from near one extreme to near the other in various paragraphs. For instance, on page 30 we are told: "There is no need to assume the existence of genes which would make one like or dislike pork; it is all a matter of conditioning or habit." With this general idea biologists can have little, if any, quarrel. What sticks in the reviewer's craw is the little word, "all." In view of what we already know about the genetics of tasting such things as P.T.C. and the partially genetic basis of some food-allergies, "all" takes in too much territory. The reviewer is happier with such wording as appears two pages later in discussing whether persons differ genetically in ability to make the sounds peculiar to certain languages. After stating that the hypothesis cannot be dismissed out-of-hand; although it certainly has never been proved, he says: "It is mentioned here chiefly to stress the fact that there is no incompatibility between genetic and cultural conditioning. A phoneme may be due to both and though anyone can learn a click, at least as a child, some people may conceivably find doing so easier than others."

The author's willingness to give his guarded but best appraisal of important situations where the facts are still not all clear is refreshing and might well be emulated by others writing for a general audience. In this respect his motto may well have been this sentence on page 9: "But, while it is dangerous to forget the extent of our ignorance, it is foolish to neglect what we know."

The subjects of the five chapters may be paraphrased thus:

1. Man as a product of evolution; the nature of heredity.

2. Cultural evolution, as distinct from biological evolution; what part heredity plays in cultural evolution.

3. What is "fitness," anyhow? Reproductive success; cooperation as well as competition; stability of phenotype, in spite of variable environments, is often desirable.

4. Human and animal societies; the detailed behavior of social insects is almost wholly gene-determined, but man's genes give him the capacity to learn from his culture and his long childhood gives him time to do so.

5. To what extent is man free to choose how he will act? Evolutionary ethics; how can man hasten his own evolution if he doesn't know the direction in which it is going? The important of ethics devolves from man's ability to choose freely between ideas and between acts.

Strangely, random genetic drift is not mentioned as a factor in evolution or in causing racial diversity. Indeed on page 115 we read: "....that, until recently, most anthropologists and biologists failed to realize that *most of the racial traits in man are adaptive*, and consequently they did not direct their investigations towards finding the adaptive functions of these traits." The italics are the reviewer's, who still doubts that selection in different directions in different localities had *much* to do with causing human racial diversity, except as it exercised mildly a remote veto.

Also missing was any mention of how the effective size of inter-breeding population can reverse the net selection coefficients for or against genes which encourage an individual to sacrifice himself when that will promote the good of his group. Such gene-conditioned heredity in insects is mentioned in Chapter 4 in some detail. Fisher nearly 30 years ago emphasized how, in tribal societies, "the blood tie" and the social approbation in which the hero's relatives would bask, could operate to select for any genes promoting intelligent heroism and self-sacrifice. Wright's quantitative exposition of the consequences of "effective size" of the interbreeding population showed how the net selection pressure, even without conscious social approbation, is likely to be for such genes in small societies but will turn against them in societies so large that the survivors, whose welfare was promoted by the hero's self-sacrifice, would be only slightly related to him; i.e. would have few of the genes which distinguished him from the more selfish or cowardly members of his group. This important, but not widely known, role of population size might well have been mentioned in a book dealing so much with ethics and human behavior and human evolution.

The reviewer doubts strongly the *general* truth of the statement on page 113: "With man, cultural developments have served to equalize, rather than to diversify, the environments of the human races, irrespective of the geographical differences, since man has gradually learned to create his own environment wherever he lives. To become adapted to a colder climate, a race of animals grows warmer fur, and becomes genetically different from races which live in warmer climates. Man meets the same situation by building bigger fires and designing warmer clothes." The example cited is well chosen but surely the changes in human culture must have made many of the selection coefficients for behavioral traits change markedly from one cul-

ture to another. Imagine how vastly different must have been the mental and emotional qualities which made for biological success among the aboriginals in Australia, the ancient Greeks, the Aztecs in Mexico, the Norse vikings, the frontiersmen around Daniel Boone, and the factory mechanics in Detroit!

Biologists will not get much from this book which isn't in Jennings or Simpson, except for a bit more philosophy about ethics and culture. The general public, less likely to have read Jennings or Simpson, will get a mostly wholesome and well-rounded view of the relation of man's "culture" to his heredity. This is in spite of some swinging of emphasis from one extreme to another. Such swings are generally corrected or balanced by swings in the opposite direction elsewhere, but not always in juxtaposition where the reader would be likely to put the whole in balance.

In spots, as on page 112 where the reference to Weidenreich points out "the remarkable fact" that "there is no evidence," the unwary reader may well be misled as to whether something (1) has been proved not so, (2) has not been proved so, or (3) has been proved so. To promote clear thinking on such matters, statisticians long ago introduced "the null hypothesis." This seems to many of us a peculiarly awkward way of backing into a question; yet experience seems to prove it necessary if confusion about what is proved is to be avoided. Jennings treats of specific forms of such confusion in his "biological fallacies, Nos. III, VIII and IX."

Probably no author can safeguard his readers from all possible misinterpretations, especially when he tackles a broad and tangled subject and must be this brief. In this case the nature of the audience generally barred the use of formulas, equations or other quantitative forms of statement.

P.S. I liked this book. A few bits of it I didn't like but anyway it was fun to explore the reasons for that!

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ON THE ORIGIN OF THE MALE TORTOISESHELL CAT

TAKU KOMAI AND TAKAAKI ISHIHARA*

THE origin of the male tortoiseshell cat has long been a perplexing problem to the geneticist. Several hypotheses have been proposed, but none of them has obtained universal support[1]. Komai became interested in this problem some years ago, and has collected material from various sources. His hypothesis to account for the origin of such cats was published in 1952[14], and was presented at a session of the XIV International Zoological Congress in 1953. More recently, he suggested that Ishihara investigate histologically and cytologically the testes of some such cats. This study has yielded some interesting results. It is the purpose of this paper to report these findings, and to present the hypothesis which seems to explain the origin of these exceptional cats.

Genetics of Common Coat Colors in Cats

It is now beyond question that the gene for orange color O in cats is sex-linked, whereas the gene for tabby (b^+) or black (b) is autosomal. This has been ascertained by simple analysis of the results of a census of cats conducted in some towns of Japan.[13] The observed relative frequency of the genes for common coat colors among the population of cats agrees perfectly with the relative frequency expected from the above assumption. Much the same thing was found by Searle[20] who carried out a similar survey of cats in London. The only difference between Searle's finding and those presented here is seen in the incidence of O which is 10.69 percent in the London cats and from 25 to 40 percent in the Japanese cats. Searle, in a recent personal letter from Singapore where he is now stationed, has communicated to Komai that the incidence of O among Singapore cats seems to be about as high as among Japanese cats.

The effect of O, either in the homozygous O/O state, or in the hemizygous state $O/$, completely covers the effect of the autosomal gene for black, b or tabby, b^+, and produces an orange coat, while in the heterozygous state O/O^+, it allows the effect of the latter gene to appear partially—hence the tortoiseshell coat. The genetic formulae of common coat colors in cats may be written as follows:—orange female = O/O b/b (or b/b^+, b^+/b^+); black female = $O^+/O^+b/b$; tabby female = $O^+/O^+b^+/b^+$ (or b/b^+); tortoiseshell female = $O/O^+b/b$ (or b/b^+, b^+/b^+); orange male = $O/$ b/b (or b/b^+, b^+/b^+); black male = $O^+/$ b/b, tabby male = O^+ b^+/b^+ (or b^+/b).

Specimens of Tortoiseshell Males

The Japanese people have a great interest in tortoiseshell male cats, because there is a current tradition that such a cat brings the owner good luck and security. Therefore the news of the birth of such a kitten often appears in local papers. Through such reports as well as through personal communication, Komai has been able to collect records of 65 animals which are apparently real tortoiseshell male cats. Whenever news of such a cat reaches him, he sends a printed figure of an extended cat's skin to the owner, with the request to make a color sketch of the animal. It is very easy to judge from the sketch whether the cat is a real tortoiseshell or a tabby as it is sometimes erroneously diagnosed. If the owner lives in a local vicinity, Komai or his assistant visits the home of the owner, and examines the specimen. In no case has Komai found his preliminary diagnosis based on the sketch wrong by actual examination. Twenty-four specimens out of the total 65 were thus examined. The information of coat color of the mother, father (though this is often unknown or dubious) and of litter mates was also obtained as far as possible.

From these data, it has been clear that the mother of a tortoiseshell male can be of any color. However, her color and the color of her

*Contribution No. 165 from National Institute of Genetics, Misima, Japan.

TORTOISESHELL MALES

Figure 10

Left—A tabby sterile tortoiseshell male (specimen No. 4). Right—An apparently fertile tabby tortoiseshell male (specimen No. 65).

mate, and the color of her progeny should represent one of the relationships shown in Table I.

The tortoiseshell male has much the same pattern as the tortoiseshell female. In disposition and behavior they are generally timid, and keep away from other males. They seldom show any sign of sexual interest in the breeding season. Their testes are considerably smaller than normal, and have a more solid consistency. There are a few exceptions to this rule, in which the male shows sexual interest in breeding seasons, chases the female and copulates. Such males which have been observed , as well as those recorded in the literature, will be described below.

Histo-cytological Observations on Testes of some Tortoiseshell Males

These studies were made by Ishihara. The material was fixed in Bouin's or Champy's fluid, and sections were cut by the ordinary paraffin method. Squash technique with pretreatment of the material with hypotonic Ringer's solution was found suitable for chromosome observation.

a. *Testes of sterile tortoiseshell males*

The testes of four apparently sterile tortoiseshell males available for study were fixed in various seasons. These testes are nearly identical in structure. The majority of seminal tubules are smaller than those in normal testes, and present a distinct vacancy inside. The interstitial tissues are rather well developed. In one specimen, the tubules are entirely lacking in germ cells. In two specimens, the tubules contain a few germ cells besides some Sertoli cells arranged near the periphery (Figure 11). The germ cells which are apparently in the spermatogonial stage, show signs of pycnotic degeneration. In the fourth specimen, the germ cells seem to be in the secondary spermatocytic stage, and present a similar degenerative change. These observations agree with the descriptions of the histology of testes of tortoiseshell males given by previous authors[6,18].

b. *Testes of apparently fertile tortoiseshell males*

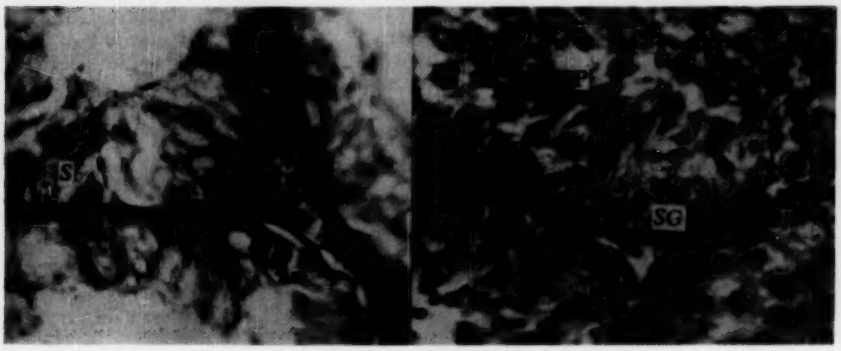
Two specimens of tortoiseshell males examined by Ishihara had testes which appeared histologically quite normal in every respect. The seminal tubules are thicker and stuffed with germ cells in various stages of spermatogenesis. The spermatogonial cells are piled up in several layers. There were many cells in primary or secondary spermatocytic stage, also spermatids and spermatozoa in large numbers and appearing quite normal.

Intensive cytological studies on these materials have revealed that the diploid chromosome complex is made up of 38 chromosomes including a distinctly unequal X-Y pair. The haploid complex consists of 19 chromosomes. (For further details, see Ishihara[11]). Ishi-

TABLE I. Interrelationships among coat-colors of parents and progeny

Mother	Father	Daughters		Sons	
		Regular	Exceptional	Regular	Exceptional
Black*	Orange	Tort.	Black	Black	Tort.
Orange	Black	Tort.		Orange	Tort.
Tort.	Orange	Tort., Orange	Black	Orange, Black	Tort.
Tort.	Black	Tort., Black		Orange, Black	Tort.

*Black represents both Black and Tabby.



SEMINAL TUBULES
Figure 11

Left—Cross sections of seminal tubules from specimen No. 4. 300×. *S* = Sertoli cells. Right—Cross sections of seminal tubules from specimen No. 65. 300×. SG = Spermatogonia, SP = Spermatozoa.

hara's study has confirmed the presence in these cats of a normal chromosome complex of a male cat, as given by Minouchi[16], Minouchi and Ohta[17], and Makino and Tateishi[15].

Observations on Three Specimens of Apparently Fertile Tortoiseshell Males

Both of the tortoiseshell male cats which provided Ishihara with apparently normal and fertile testes had been kept in a home in Misima, and their behavior had been under observation by the owners. They showed sexual interest in breeding season, chased females, and one of them was once seen in coitus with a female. Although their fertility had never been confirmed, it is likely they were fertile. They were both typical tortoiseshells, one a black-tortoiseshell and the other a tabby-tortoiseshell (Figure 10), and had no outward characteristic to separate them from ordinary tortoiseshell males except for the behavioral difference.

The third specimen of an apparently fertile tortoiseshell male is a pet in the home of Prof. S. Hashioka of Hiroshima University. Komai examined it and confirmed it to be a beautiful tabby tortoiseshell male specimen. Hashioka has seen it in coitus with a female. One of his neighbors, a housewife who keeps a tabby tortoiseshell female, confined her female with Hashioka's male in a barn in a breeding season of 1954. The female became pregnant, and gave birth to a tortoiseshell male kitten besides two orange and one tortoiseshell female. Although this is neither our own observation, nor Prof. Hashioka's, the information is highly suggestive, together with Hashioka's observation of coitus, of the actual fertility of this tortoiseshell male.

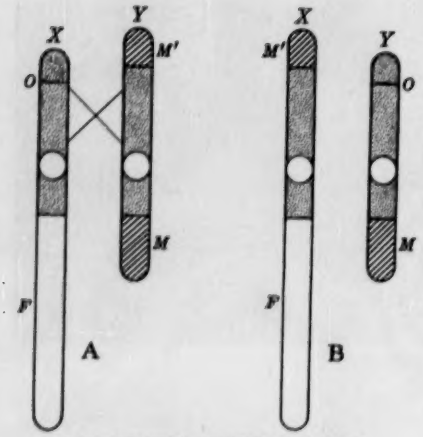
The Origin of Tortoiseshell Males

It seems clear from Table I, that the exceptional tortoiseshell males are heterozygotes of the gene for orange, $O/O+b/b$ (or $b+/b+$, $b/b+$), much the same as tortoiseshell females. Since O is a sex-linked gene, either O or $O+$ should be located in the Y-chromosome. This could happen, if O is only partially sex-linked, and transferred occasionally from X to Y by crossing-over, and the Y which carries O or $O+$ meets in fertilization an X which carries its allele $O+$ or O.

Koller[12] has formulated a detailed structure of the X- and Y-chromosomes in cats. He maintains that these chromosomes are nearly equal in length, and are both differentiated into pairing and differential segments, and chiasma may be formed between the corresponding pairing segments of X and Y. Other authors find a distinctly unequal X-Y pair. For our purpose it is sufficient if each of these chromosomes is differentiated into a pairing and a differential segment, with crossing-over possibly taking place between the pairing segments.

There remains the question of sterility which is the general rule of such males. Of the 65 specimens collected by us, only three were probably fertile. To account for this remarkable peculiarity of the tortoiseshell male cat, it seems necessary to assume the presence of a gene or gene complex governing fertility of the male in the Y-chromosome, and its transfer to X by crossing-over, reciprocal to the transfer of O from X to Y. So far the presence of such a gene or gene complex in the Y-chromosome of a mammal has never been demonstrated. It seems plausible, however, that some day when the structure of mammalian Y-chromosomes are more minutely investigated, the presence of such a gene complex will be demonstrated.

Concerning the origin of the rare fertile tortoiseshell males, it is conceivable that, if crossing-over between X and Y transfers O from X to Y, but fails to remove from Y the



SCHEMATIC ORIGIN OF THE TORTOISESHELL MALE

Figure 12

F = differential segment of the X-chromosome, M = differential segment of the Y-chromosome, M' = the section containing a gene complex for fertility of the male, O = the gene for orange color.

gene complex for fertility, then a fertile tortoiseshell son may result. Such a son should produce among its progeny some tortoiseshell males which are likewise fertile. Prof. Hashioka's tortoiseshell male perhaps represents such a case, as it produced a tortoiseshell son among its progeny.

There are a few records of fertile tortoiseshell males in the literature (Doncaster[7, 9], Cutler and Doncaster[6], Bamber and Herdman[3]). A detailed and reliable siring record is given by Bamber and Herdman[2-4] of their pet "Lucifer", a tortoiseshell male. This cat sired as many as 56 kittens by three females. In general, this male behaved almost like an orange, except for its three progeny which had some black hair. This record of "Lucifer" is understandable, as indicated by Bamber and Herdman, only by assuming that he was a genotypical orange, but that the epistatic effect of O over b was hindered to some extent by a modifying gene, or by some other cause, thus producing a tortoiseshell phenotype. The specimens of tortoiseshell males examined by us which were apparently fertile, were perhaps the same kind of abnormal cats.

If this was the case, then we seem to have to admit the dual origin of tortoiseshell males: namely, the majority of such cats are produced by crossing-over between X and Y chromosomes, and they are sterile nearly without exception; the minority are genotypical oranges in which the epistasis of O is imperfect, and allows part of a black area to appear; such tortoiseshell males are fertile.

Discussion

It is to be noted that the crossing-over hypothesis which has been put forward to explain the origin of the tortoiseshell male is nothing new. Essentially the same hypothesis has been proposed by Doncaster[9], Hayes[10], Tjebbes and Wriedt[22], Crew[5], and Plate[19]. This hypothesis can also account for the birth of exceptional black females from the mating of a black or tortoiseshell female with an orange male, a phenomenon which has also been perplexing in cat genetics (Doncaster[8], Bamber[1]). If crossing-over takes place between X and Y in the spermatocyte of the orange father, then the X will lose its O gene. If an egg which bears $O+$ in its X-chromosome is fertilized by a sperm which bears no O in its X, a black daughter will be produced ("Exceptional daughters" in Table I).

It would be very difficult to present cytological evidence either for or against this hypothesis; Ishihara's intensive study has failed to demonstrate anything for or against it. However, it would be nearly fatal to the hypothesis if conclusive evidence be given that more than one tortoiseshell male may be born of one and the same mother. As a matter of fact, Komai has been informed more than a dozen times of such an occurrence. However, on examination, he found these reports in every case to be due to erroneous diagnosis of the coat color—tabby kittens were mistaken for tortoiseshells.

No previous author has succeeded in explaining the sterility of tortoiseshell males For this, it seems unavoidable to postulate the presence in the Y-chromosome of a gene or gene complex governing fertility of the male which is lost by crossing-over. In *Drosophila*[21], as well as in the plant *Melandrium*[23-26], the presence in the Y-chromosome of a gene complex governing fertility is known, although its transfer to X by crossing-over does not seem to have been demonstrated. Koller[12] suggests a similar view on the origin and sterility of tortoiseshell males, although he uses a rather vague sentence.

Bamber and Herdman[4] assume, for their fertile tortoiseshell male "Lucifer", that it probably had an additional piece of X attached to the regular X, and that the former carried $O+$ while the latter carried O. To us, the presence of a modifying gene or gene system seems to be a simpler and more plausible assumption than the duplication of genes for coat color.

Summary

Analysis of the results of a census of cats in some Japanese towns has shown that the gene for orange color (O) is sex-linked whereas the gene for black (b) or tabby ($b+$) is autosomal. The incidence of O is much higher among Japanese cats than among London cats.

Based on reliable records of 65 tortoiseshell males, together with the data on their mothers,

fathers and litter mates, it has been found that the mother of a tortoiseshell male can be of any color, but that her color and the color of her mate and progeny should represent one of the relationships presented in Table I.

Histo-cytological studies were made on testes of six tortoiseshell males. Four of these cats had sterile testes which indicated arrest of spermatogenesis in the spermatogonial or spermatocytic stage. The remaining two cats had apparently fertile testes which were normal in every aspect. The chromosome complex contained in the germ cells consisted of 19 pairs of chromosomes including an unequal X-Y pair.

Observations on the outward appearance and behavior of the tortoiseshell males are described. The majority of them appear to be somewhat deficient in masculinity; they seldom show sexual interest in breeding season; their testes are underdeveloped and sterile. Three specimens, including those which had histologically normal testes, showed sexual interest. One of them was once kept in confinement with a female in a breeding season, and sired kittens.

The tortoiseshell male is a heterozygote for the gene O (O/O^+), like a tortoiseshell female. The Y-chromosome of such a male apparently carries O (or O^+) which is ordinarily not present in that chromosome. This would be possible, if X and Y have pairing segments and crossing-over takes place between them in the spermatocyte of the father, and transfers O (or O^+) from X to Y.

Sterility of most of the tortoiseshell males can be explained by assuming a gene or gene complex controlling fertility of the male present in the Y-chromosome, and its transfer by crossing-over from Y to X, reciprocal to the transfer of O from X to Y.

Records of fertile tortoiseshell males in the literature are reviewed. The origin of such fertile tortoiseshell males is considered. At least a part of them seem to be genotypical oranges in which the espistatic effect of O is imperfect, and allows some black hair to appear.

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THE ACADEMIC ORIGIN OF DROSOPHILA WORKERS IN THE UNITED STATES

J. Alfred Chiscon*

In May of 1906 an article written by W. E. Castle and his students appeared in the Proceedings of the American Academy of Arts and Sciences[3]. It presented results of experiments begun five years previously on the effects of inbreeding, cross-breeding and selection upon fertility and variability of *Drosophila melanogaster*. This fast-breeding fly was used by the authors as the experimental organism because it was present in the laboratory at the time, being cultured there by a graduate student as embryological material[6].

This paper turned the attention of T. H. Morgan to *Drosophila* as a possible new source for experimentation. Extensive utilization of the fly in subsequent years has raised it from a position on fruit store produce to the honor of having contributed more to our knowledge of the physical basis of heredity than any other organism[10].

The fifty years following Castle's paper finds thousands of significant reports involving *Drosophila* in the scientific literature. These papers have come from workers scattered in laboratories throughout the world, a generous percentage being from within the confines of the United States. The present paper summarizes recent investigation undertaken to determine the academic origin of the *Drosophila* workers in this country with respect to the place of attainment of their baccalaureate and doctoral degrees.

The greater portion of the list of scientists upon which this report is based was secured from the *Bibliography on the Genetics of Drosophila*[2] as compiled by H. J. Muller and I. H. Herskowitz. These two volumes contain 5,806 titles and cover the *Drosophila* field through 1950 with a high degree of thoroughness. Names of additional workers who obtained doctorates since 1950 and through 1954 were obtained by surveying the literature of leading journals publishing in the field of genetics during this span of time. The investigation as a whole was sufficiently inclusive to keep possible omissions at a minimum.

Names from the resuting list of scientists were checked individually in the volumes of *American Men of Science*[4] spanning the past fifty years. Data were accumulated as to the year and institution at which these men and women received the bachelor, master and doctoral degree. Names of people publishing in the United States but not listed in any of the volumes of *American Men of Science* were further investigated in the issues of *Drosophila Information Service*[5]. Names which could not be located following this procedure were considered to be foreign residents.

From this compiled list of American *Drosophila* workers, those who had ob-

TABLE I. Doctoral origin of U. S. *Drosophila* workers through 1954

Name	No. of Doctorates	Name	No. of Doctorates
Columbia	76	Northwestern	3
Harvard	59	Stanford	3
Texas	40	Bryn Mawr	2
California	28	Kansas	2
Chicago	28	Oklahoma	2
Hopkins	25	Pittsburgh	2
Illinois	21	Purdue	2
Cal. Tech.	20	Radcliffe	2
Pennsylvania	19	Rice	2
Cornell	17	Rutgers	2
N. Y. U.	14	West. Reserve	2
Missouri	11	American	1
Wisconsin	11	Barnard	1
Yale	11	Catholic	1
Michigan	9	Cincinnati	1
Iowa State	8	Louisiana	1
Minnesota	7	Maryland	1
Ohio State	6	M. I. T.	1
Washington (St. Louis)	6	Michigan State	1
Indiana	5	Nebraska	1
Princeton	4	Oregon State	1
Rochester	4	Smith	1
Iowa	3	Tennessee	1
		Utah	1
			471

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tained their doctorate were selected and the instiutions at which they received this degree and their undergraudate degree were noted. Tables I and II summarize the result of this investigation. In cases where more than one undergraduate degree was obtained by the same person, the date and place of the first to be awarded was used. Where both an M.D. and Ph.D. were obtained by the same person, the Ph.D. data were utilized. When an M.D. alone was obtained, the information for that degree was used. Cases in which such a choice of institutions had to be made were exceedingly few.

A few less bachelor degrees (440) than doctorates (471) were noted since some undergraduate degrees were obtained abroad while no record could be found of the others. Although information concerning the masters degree was also obtained, it is considered incomplete since many scientists did not include this information or the degree was bypassed in work toward a doctorate.

Of the 471 doctorates from 47 institutions, 71.1 percent came from the first ten schools listed in Table I. Nearly one-half of the doctorates (49.0 percent) were awarded by the first five schools listed: Columbia, Harvard, Texas, Cali-

TABLE II. Baccalaureate origin of U. S. *Drosophila* workers through 1954

Name	No. of Degrees	Name	No. of Degrees	Name	No. of Degrees
California	19	Ala. Polytech.	2	Hunter	1
Texas	19	Allegheny	2	Illinois Col.	1
Columbia	17	Barnard	2	Ind. Cent. Col.	1
Harvard	16	Berea	2	Kentucky S.T.C.	1
City of N. Y.	13	Boston	2	Linfield	1
Illinois	11	Bryn Mawr	2	McPherson	1
Indiana	11	Denison	2	Maine	1
Dartmouth	9	Emory	2	M. I. T.	1
Kansas	9	Hamline	2	Mich. Col. Mines	1
New York Univ.	9	Iowa STC	2	Middlebury	1
Wisconsin	9	Kentucky	2	Millikin	1
Michigan	8	Lake Forest	2	Mississippi	1
Cornell	7	Marquette	2	Monmouth	1
Hopkins	7	N. Central	2	Montana	1
Missouri	7	Oregon State	2	Moravian	1
Mt. Holyoke	7	Penn State	2	Nazareth	1
Yale	7	Pomona	2	New Hampshire	1
Pennsylvania	6	Reed	2	No. Carolina	1
Wooster	6	Rochester	2	No. Dak. Col.	1
Baylor	5	Smith	2	NW Mo. STC	1
Brooklyn	5	Swarthmore	2	Park	1
Cal. Tech.	5	Texas A&M	2	Phila. Col. Phar.	1
Chicago	5	Ursinus	2	Phillips	1
Amherst	4	Utah	2	Radcliffe	1
Bates	4	Valparaiso	2	Regis	1
Minnesota	4	Washington (St. Louis)	2	Rice	1
Princeton	4			Richmond	1
Southwestern (Kansas)	4	Washington (Seattle)	2	Ripon	1
Wellesley	4	Washington State	2	Roanoke	1
West. Reserve	4	Albertus Magnus	1	St. Vincent	1
Franklin & Marshall	3	Alfred	1	San Diego	1
Goucher	3	Annapolis	1	San Marcos S.T.C.	1
Haverford	3	Austin	1	Simpson	1
Indiana STC	3	Boudoin	1	Shorter	1
Iowa State	3	Brooklyn Polyt.	1	So.Carolina	1
Kansas State	3	Brown	1	So. Car. A&M	1
Mass. State	3	Buffalo	1	So. Dakota	1
Michigan State	3	Butler	1	So. Dakota State	1
Nebraska	3	Central (Mo.)	1	Southwestern (Tenn.)	1
Northwestern	3	Clark	1	SW Texas STC	1
Oberlin	3	Conn. State	1	Temple	1
Ohio State	3	Dickinson	1	Tennessee STC	1
Okla. A&M	3	Drury	1	Texas Christian	1
Oregon	3	Dubuque	1	Tex. Col. for Wom.	1
Pittsburgh	3	Florida	1	Trinity	1
Purdue	3	Geo. Washington	1	Utah St. Ag. Col.	1
Rutgers	3	Grinnell	1	Va. Polytech	1
Stanford	3	Gustavus Adolphus	1	Wayne	1
Syracuse	3	Harding	1	Wesleyan (Conn.)	1
Tufts	3	Hobart	1	Whittier	1
Virginia	3	Hood	1	Wilmington	1
Alabama	2	Houston	1	Wyoming	1
					440

fornia and Chicago. A distribution of these degrees by decades is presented in Table III.

Columbia and Harvard were most active between the years 1910-19. Harvard's graduates have steadily decreased in number to the point where no doctorates as yet are recorded for the present decade. Columbia, however, has advanced its graduate number in recent years, awarding more doctorates in the decade containing World War II than during the years 1930-39. The past five years have seen nearly as many Ph.D. degrees granted at Columbia as in the previous 10, indications being that this decade will be the most fruitful in the institution's history so far as graduate numbers are concerned.

Texas, California and Chicago all reached their height of output during 1930-39, well after that of Harvard and Columbia. All three dropped during the war years of the next decade. Chicago, however, dropped at an extreme rate and has not yet approached her pre-war status. Of the five schools leading in graduates, Texas was the last to begin awarding doctorates, not doing so until after 1920. The 10 years following 1930, however, saw her awarding more doctorates than any of her four sister institutions. The University of California also appears as if it will surpass its past graduate number during the present decade.

It is obvious that the undergraduate origin of *Drosophila* workers is much more widely spread than their doctoral origin. Table II lists 155 schools for the baccalaureate, more than three times the number listed for the doctorate in Table I. The first 10 schools in Table II awarded only 30 percent of the total number of bachelor degrees, a figure which does not approach the 71.1 percent computed for Table I. The ten institutions leading so greatly in doctoral output, furthermore, presented only 25.2 percent of the undergraduate degrees.

Tables I and II further show that the first four undergraduate institutions are also the first four graduate institutions. The College of the City of New York, not appearing at all in Table I, maintains fifth position at the bachelor level. Ten of the bachelor degrees were awarded by state teachers colleges. Land grant institutions awarded 113 or 24 percent of the doctorates and 105 or 23 percent of the baccalaureate degrees. This is approximately one-half the percentage reported by Greulach[7] in his recent study of academic origin of American botanists. He found that 43.5 of the botanists in the United States received their undergraduate degree and 54.1 percent received their doctorate at land grant institutions.

It is interesting to note that, of the first 50 institutions listed by Knapp and Goodrich[8] in order of the magnitude of their productivity indexes for scientist output during the baccalaureate years 1923-34, 22 are contained in the baccalaureate list of *Drosophila* geneticists (Table II). These colleges include institutions such as Reed, Central of Missouri, Haverford and Grinnell. Sixty-eight future *Drosophila* workers were graduated from these 22 institutions.

Of the 10 institutions leading in the presentation of baccalaureate degrees to biology doctorates from 1936 through 1945[1], only three (California, Wisconsin and Illinois) are among the first 10 institutions in Table II. Furthermore, the 10 institutions presenting 30 percent of the 440 baccalaureate degrees obtained by *Drosophila* workers (Table II) awarded only 9.2 percent of the undergraduates degrees obtained by biology doctorates (1936-50).

The data for the 10 institutions presenting 335 of the 462 doctorates (Table I) were examined to determine how many of these graduates received both their baccalaureate and doctoral degrees at the same university. Results are tabulated in Table IV. The range is from 10.7 percent for California to the high, 42.5 percent, for Texas.

The 440 bachelor degrees and 471 doctorates were assembled as to the decade in which they

TABLE III. Distribution by decades of doctorates awarded by five leading institutions

Year	Columbia	Harvard	Texas	California	Chicago
to 1900	0	6	0	0	1
1900-09	1	2	0	0	6
1910-19	21	18	0	1	2
1920-29	16	10	2	5	4
1930-39	10	15	18	7	12
1940-49	15	8	11	6	1
1950-54	11	0	7	6	2

TABLE IV. Doctorate and baccalaureate degrees completed at the same institution

Institution	Total Ph.D. No.	No. obtaining both degrees from same institution	Percentage
Columbia	76	16	21.1
Harvard	59	8	13.6
Texas	40	17	42.5
California	28	3	10.7
Chicago	28	10	35.7
Hopkins	25	5	20.0
Illinois	23	4	17.4
Cal. Tech.	20	4	20.0
Pennsylvania	19	6	31.6
Cornell	17	3	17.6

were obtained. Results are presented in Table V. For both degrees it is evident that they were granted in increasing numbers until the decade involving World War II. The decreased number of degrees during this decade is in agreement with the Steelman Report[11] which indicates a very marked decline in the number of Ph.D's in science granted from 1941-47. Columbia, however, produced more doctorates during the 10 year period involving the war than it did during the previous decade.

Those institutions from which the *Drosophila* workers received their baccalaureate degrees were arranged as to the size of enrollment. The results of this tabulation is given in Table VI. The majority (58.4 percent) of undergraduate degrees were obtained at institutions having enrollment figures of less than 10 thousand students. Eighty scientists graduated from colleges containing less than one thousand students. It is obvious that both the small college and the large university have been fruitful sources of *Drosophila* workers.

The vast mapority (81.6 percent) of presently active *Drosophila* workers may be found in colleges and universities. The list of *Drosophila* geneticists was checked against the addresses of members of the Genetics Society of America[9]. The results of this survey are presented in Table VII. More than one-half (52.1 percent) of the scientists located in this manner are presently at state supported colleges or universities. Only 18.4 percent are at government, industrial, or private research laboratories.

Ten universities, then, can account for nearly three-fourths of the doctorates received by *Drosophila* workers in the United States. Five institutions can claim half of the total doctorate number. The scientists receiving the degree probably did their undergraduate work elsewhere, the majority at places having enrollments of less than 10 thousand and one-fourth of them at land grant institutions. Though far greater in number than the doctorate granting institutions, the baccalaureate colleges and universities are still a small percentage of the approximately one thousand senior institutions in the United States.

Institutions leading in doctoral graduates also lead in the baccalaureate field. This is in agreement with the report of the National Academy of Science[1], which ranked institutions as to total production of baccalaureates and doctorates in science for the period 1936-50. The field of *Drosophila* research has definitely been an increasing one. Most of the *Drosophila* geneticists are doing this research in colleges and universities. There are indications (Table V) that the present decade will compare favorably if not surpass other periods in turnout of *Drosophila* workers in the United States.

TABLE V. Distribution by decades of baccalaureate and doctoral degrees

Year	Baccalaureate Degree	Doctoral Degree
to 1900	24	10
1900-09	11	16
1910-19	82	57
1920-29	111	85
1930-39	125	141
1940-49	59	101
1950-54	6	59
	440	471

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TABLE VI. Size of institution in relation to number of baccalaureates

Enrollment	Institutions	No. of Baccalaureates Awarded	Percentage
Below 1,000	52	80	18.2
1,000-5,000	48	92	20.9
5,000-10,000	26	85	19.3
above 10,000	29	183	41.6
	155	440	100.0

TABLE VII. Present location of active *Drosophila* workers

Location	Number	Percentage
State Colleges and Universities	99	52.1
Private Colleges and Universities	56	29.5
Government Research Laboratories	8	4.2
Industrial Research Laboratories	5	2.6
Private Research Laboratories	22	11.6
	190	

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◆

Forty Faculty Awards for Research in Biology for the Summer of 1957

THE Lalor Foundation recently announced details of the 40 awards which it is offering to younger college and university staff and faculty members for research in the biological sciences for the summer of 1957. This is the third annual series of such summer research awards.

The awards are for advanced study and research employing chemistry or physics to attack problems in any field of biology. The studies may be carried on at any institution of the award holder's choice. The upper age limit for appointment is 40 years.

The awards will usually not exceed $900 for a single man or woman, $1,100 for a married person working at his home institution, and $1,250 for a married person whose principal program is at another institution. Transportation and other expenses are for the account of the award holder.

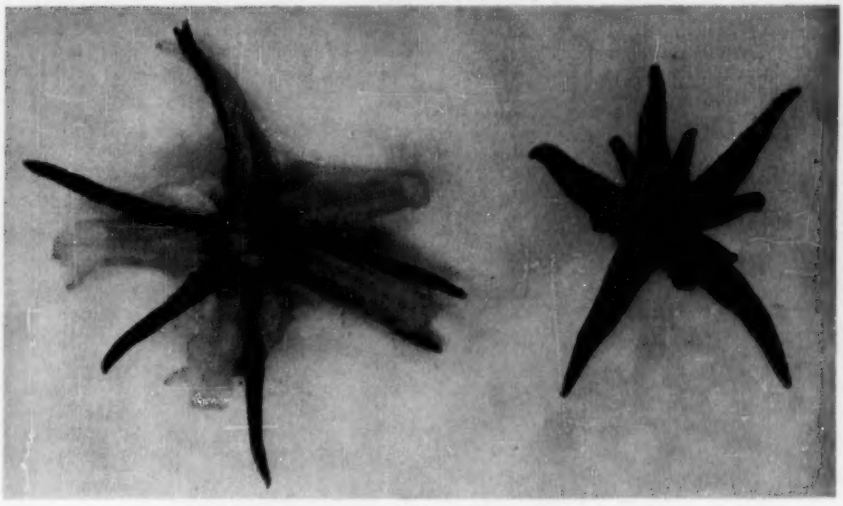
Younger faculty members with important teaching obligations find in many cases that the summer months between the academic years are the only uninterrupted periods available to them for carrying on fundamental research of their own choosing. The Lalor Faculty Summer Research Awards are designed to assist such men and women and thereby add to their standing as scientists and effectiveness as teachers.

In recent years the Foundation has maintained a number of post-doctorate summer fellowships at the Marine Biological Laboratory at Woods Hole, Mass. With the consolidation of these fellowships into the present program, it is suggested that men and women interested in work at M.B.L., and eligible under the Lalor faculty summer award plan, should submit applications under this newer program.

Inquiries respecting Lalor Faculty Summer Research Awards should be addressed to the Director of the Lalor Foundation, 4400 Lancaster Pike, Wilmington 5, Delaware. Final date for receipt of completed applications is January 14, 1957, and notification regarding appointment may be expected by March 15, 1957.

A STAMENLESS TOMATO MUTANT WITH ABNORMAL COROLLA

L. HAFEN AND E. C. STEVENSON*



NORMAL AND STAMENLESS TOMATO FLOWER

Figure 13

Left—Normal tomato flower. Right—Smaller mutant flower, showing the stamenless condition and the rough and irregular stigmatic surface.

A MUTANT tomato plant was discovered in a commercial field planted to the Rutgers tomato variety. The corolla was green and sepal-like in appearance, and smaller in size than the sepals. Stamens were not produced and the stigmatic surface was rough and irregular (Figure 13).

Cuttings of the plant were taken and rooted in sand in the greenhouse. The mutant plants were then crossed with fertile plants of the Pritchard variety. Fruit set and seed per fruit from crosses on the mutant plants were poor indicating that a high degree of female sterility was associated with the abnormal flower type.

Flowers of F_1 plants were nearly normal. The petals were yellow, but there appeared to be some interference with normal anther development, particularly with the first flowers, a condition which was not evident in commercial fertile varieties that were growing in adjacent rows. The flowers ranged from vestigal to normal in anther development. As plant growth progressed and temperatures increased, all flowers of the F_1 plants had normal anther development. There was no female sterility evident in these plants.

An F_2 population segregated 305 plants with normal petal color, near-normal anther development, and female fertile, and 120 plants with green corolla, stamenless, and with a high degree of female sterility. Similarly a backcross progeny segregated in a ratio of 26 plants with normal petal color, near-normal anther development, and female fertile to 19 stamenless plants, with green corolla, and a high degree of female sterility. The segregations gave a good fit to a 3:1 and a 1:1 ratio respectively indicating that the mutant condition is controlled by a single recessive gene, and the gene symbol, *cs*, has been assigned to it.

In these studies near-normal anther development was always associated with yellow petals and missing anthers with green corolla. The results of the F_2 and backcross segregations

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suggest three genetic possibilities; (1) The genes for stamenless, sepal-like corolla, and female sterility are very closely linked; (2) a single gene is responsible for the pleiotropic phenotypic expression; and (3) a portion of the chromosome carrying the genes for these three characters has been deleted. If either of the latter two possibilities is the explanation, the characters would always be associated together.

Summary

A mutant plant found in a field planting of Rutgers tomato produced flowers lacking stamens, with sepal-like anthers, and a high degree of female sterility. Mutant plants were crossed with the Pritchard variety, producing an F_1 generation with yellow corolla, near-normal anther development, and no female sterility. Segregations in F_2 and backcross populations indicated that the mutant flower condition and high female sterility are conditioned by a single recessive gene assigned symbol, *cs*.

EFFECT OF VARIETAL MASS ON PERCENTAGE OF OUTCROSSING

In *Gossypium hirsutum* in New Mexico

PAUL A. FRYXELL*

LITTLE attention has been directed to the importance of varietal mass to inter-varietal cross-pollination in entomophilous plants. Varietal mass refers to the spatial distribution of a population, its size, shape, and thus the relative extensiveness of its perimeter. Bateman[1] found that by varying the number of rows (of radishes) from one to 12, the degree of contamination was reduced for a constant isolation distance as the mass of the isolated population was increased. That is, the border plants of the isolated population evidenced a higher rate of cross-pollination (with the distant contaminant variety) than did the more centrally located plants. This border effect, however, was found to fall off sharply and to be negligible beyond about five feet from the edge of the plot. The conclusion was reached, therefore, that apart from this relatively small border, the degree of inter-varietal contamination was a function of isolation distance alone.

Preliminary data are presented herewith indicating that the effect of varietal mass may be much greater than that reported by Bateman. Consequently, the effect of varietal mass is one that must be considered in specifying population breeding structure, at least for some species, in that the degree of inter-varietal contamination is *not* simply a function of isolation distance alone.

Experimental Procedure

Two varieties of cotton (*Gossypium hirsutum*) were grown in fields immediately adjacent to each other, their rows being parallel. The surrounding fields were planted with other crops. These two varieties are essentially indistinguishable, but differ genetically at a locus, B_7,[6] conferring resistance to the bacterial blight disease (*Xanthomonas malvacearum*) on the recessive genotype†. This locus, then provides a tool for the study of inter-varietal pollination relations. Samples were taken from the field of resistant cotton and inter-varietal cross-pollination was detected as susceptible progeny‡. Three series of samples were taken, each of which was distributed in a line perpendicular to the rows. Each sample was the seed from four fruits of an individual plant. These samples were taken from each row up to the sixteenth row and at more widely spaced intervals thereafter, up to the fiftieth row. The rows were 3½ feet apart.

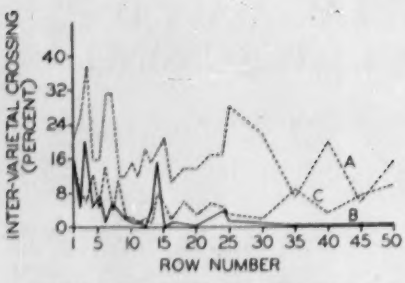
The seed samples were classified in greenhouse culture by inoculating the cotyledons of each seedling with the pathogen. The classifications were made approximately nine days after inoculation. The percent of susceptible seedlings in a sample is interpreted directly as percent of inter-varietal cross-pollination. These data are presented in Figure 14. A check of a sample of the seed used to sow the resistant field indicated that about six percent of these plants were of a susceptible genotype. Thus, some of the inter-varietal crossing indicated in Figure 14 may actually be intra-varietal crossing; however, this discrepancy is considered to be negligible. Two of the sample plants gave 65 percent and 97 percent susceptible progeny respectively. It is probable that these two plants were actually of a susceptible genotype (heterozygous and homozygous respectively); consequently these data were discarded.

The width of the field (i.e., the length of the row) was approximately 630 feet. Series A and C were taken about 150 feet from either edge of the field; series B from the center of the field. Examination of Figure 14 shows

*Department of Botany and Bacteriology, University of Wichita, Wichita 14, Kansas. The author is indebted to E. E. Staffeldt, L. M. Blank, and R. E. Hunter of State College, New Mexico for material aid in the collection of samples and to R. E. Hunter for making the classifications for disease reaction.

†Though described by Knight[6] as dominant under his field conditions, B_7 behaves as a recessive when classifying cotyledon disease reactions.

‡The conduct of this experiment was under conditions free of the bacterial blight disease.



PERCENT OF INTER-VARIETAL CROSS-POLLINATION

Figure 14

Relation of inter-varietal crossing to distance from contaminant for three series of samples.

that for series B the intervarietal crossing of the first rows immediately adjacent to the contaminant plot is comparable to the known rate of natural crossing for this species in New Mexico[6,7]. With increasing distance from the contaminant field the rate of crossing decreases, eventually leveling off at a negligible amount. For the A and C series, however, although there is a reduction in rate of crossing with distance, the rate of crossing remains fairly high even at a distance of 50 rows from the contaminant. Apparently the position of the plants relative to the border of the population, i.e., varietal mass, affects their breeding behavior. The effect of varietal mass is therefore quite appreciable for a distance of 150 feet into the field from the border, but is negligible at 315 feet. At what intermediate point this effect becomes negligible in cotton remains to be determined from future studies. However, the conclusion that this effect is important seems inescapable.

An additional effect of varietal mass can be seen from a comparison of series A and series C. It is evident that the rate of crossing is relatively higher in the former, actually exceeding the accepted rate of natural crossing. This takes on meaning when one considers the shape of the experimental field, which resembled the letter L. The top half of the perpendicular member was the susceptible (contaminant) field; the remainder of the area was the resistant (test) field. The C series was taken from the side from which the horizontal member projected; the A series was taken from the other side. The varietal mass of the projecting member evidently exerted an influence on the C series reducing the rate of inter-varietal crossing which it showed relative to the A series due to the additional "mass" of the projecting member. (The projecting member was beyond the fifty row sampling limit.)

Discussion

The analysis of variance of the transformed data is presented in Table I. It can be seen that the differences among the series is highly significant and that therefore the breeding structure of the population was not uniform. This difference at first seems attributable to the large deviation of the A series. However, partitioning the variance to provide a test of the difference between the B and C series shows that this difference is real and that the C series is exhibiting the same phenomenon (effect of varietal mass) as the A series but to a lesser degree. This difference in degree has been attributed to the influence of the projecting member of the field previously referred to, and is thus an additional effect of varietal mass. The reduction in rate of crossing with isolation distance is largely a linear relation, after angular transformation of the data. It was not possible to test the interaction, due to a lack of replication. Such interaction seems to be small, however.

Where non-uniformity of breeding structure of the type here encountered exists, one would anticipate that the approach to panmixia would be greater in the borders than in the center of the population, at least if the intrinsic rate of natural crossing were low. This supposition takes on added importance when the borders can be as wide as here indicated. The implications of this altered breeding structure, including such things as hybrid seed production, are numerous and are considered by Fryxell[4]. Experimental verification of the greater approach to panmixia near the perimeter, of course, is desirable and possible[5].

With an entomophilous crop such as cotton, non-uniformity of breeding structure must be explained in terms of the activities of the insect vectors which transfer the pollen. Such non-uniformity must result from non-uniformity of vector activity. Consequently, one must qualify the conclusion of Finkner[3] that the activity of pollen vectors in Upland cotton is at random. His conclusion is not invalidated, however, as the influence of varietal mass was not considered in his study, the border plants not being tested. Furthermore, a much larger pollen vector population was operating in his study with a consequently higher rate of natural crossing.

TABLE I. Analysis of variance of percent inter-varietal cross pollination after transformation to angles

Source	d.f.	Sum of Squares	Mean Square
Rows	25	1563.21	62.53**
Linear component	1	461.77	461.77**
Residual	24	1101.44	45.89
Series (A,B,C)	2	3705.79	1852.90**
A vs. remainder	1	3403.86	3403.86**
Among remainder (B vs. C)	1	301.92	301.92**
Row X Series interaction	50	1358.13	27.16
Total	77	6627.13	

**Significant at 1 percent probability level.

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THE LINKAGES OF CONGENITAL HYDROCEPHALUS IN THE HOUSE MOUSE

RITA J. S. PHILLIPS*

A RECESSIVE gene, symbol *ch*, causing congenital hydrocephalus in the house mouse, was first discovered by Grüneberg[2], and has been described in detail by him: this paper deals only with linkage tests made with *ch* and with its position in group XIV.

Materials and Methods

The gene *ch* was obtained from Prof. H. Grüneberg in September 1950 and tested against our linkage testing stocks[1]. *Ch* is a recessive gene lethal in the homozygous condition; the homozygotes die immediately after birth and are often eaten by their mother prior to the litters being found[2]; therefore linkage tests are not straightforward.

Three types of linkage-test matings were used:

1. The majority of tests were of the type $ch+/+m \times +m/+m$ (where *m* was the recessive marker under test), all female offspring being tested genetically for the presence of *ch* by mating to known heterozygous males. The females were sacrificed 16 days after a vaginal plug had been observed and their embryos were examined: *chch* embryos of this age are easily distinguishable from normals.

2. When the embryos from proven $+ch$ test females of the previous group also segregated in other genes classifiable at the 16 day stage, for example siderocyte anaemia, *f*, and ruby-eye, *ru*, then the embryos themselves provided further linkage data.

3. A third group of data was obtained from matings of the type $ch+/+M \times ch+/++$ (where *M* was a dominant marker under test) the females being allowed to litter. This method was only used where the marker against which *ch* was being tested was itself classifiable at birth, for example Brachyury, *T*, and Caracul, *Ca*.

In all cases only the *chch* offspring (or, with method 1, the proven $+ch$ females) were considered when calculating recombination percentages. This was done to avoid biasing the data with method 1 due to incompleteness of test of females; with method 2 due to selection of data from only those females which produced at least 1 *chch* embryo and with method 3 due to postnatal elimination.

Genetics

1. *Independence tests*

The results of the initial two-factor tests made to detect any linkages are presented in Table I. From these it can be seen that *ch* shows fairly close linkage with siderocyte anaemia, *f*, in group XIV. A slight indication of linkage was also observed between *ch* and jerker, *je*, in group XII,; the possibility that groups XIV and XII are on one chromosome cannot be excluded, but, as the data with *je* are not internally consistent, this apparent linkage is probably a chance effect only, not unexpected amongst 19 separate tests.

2. *The position of ch in linkage group XIV*

Group XIV was first discovered by Dr. J. W. B. King[3] who found that *f* showed 33.6 ± 2.6 percent recombination with crinkled, *cr*. To determine the position of *ch* in this group three-factor tests of the type $+ ch +/f + cr \times f + cr/f + cr$ were set up. The data are presented in Table II and analyzed in Table III.

Amongst the *ch*-carrying offspring it will be seen that there are no crossovers for *ch* alone, two for *cr* alone and six for *f* alone, indicating that *ch* lies between *f* and *cr*. The estimate of the *f*/*ch* recombination value from the combined two-factor and three-factor tests is about 10 percent (Table IV); this implies

*Medical Research Council's Radiobiological Research Unit, Atomic Energy Research Establishment, Harwell, England. The author is grateful to Professor H. Grüneberg, F.R.S. for the gift of mice carrying congenital hydrocephalus and to Miss H. G. Shewry for technical assistance.

that the map is:—

cr—— 8% —— *ch* —— 10% ——*f*

←———— 28% ————→

Summary

Linkage tests were carried out between congenital hydrocephalus, *ch*, and most of the known linkage groups in the mouse. It was found that *ch* lies between siderocyte anaemia, *f*, and crinkled, *cr*, in group XIV.

TABLE IV. Recombination of *f* and *ch*. Combined estimate from Tables I and II.

Total of proven + *ch* offspring	Old combinants	Recombinants	Recombination and standard error %
98	89	9	10.41 ± 3.26

TABLE I. Results of two-factor independence tests

Linkage Group	Genotype of parents	+*M*	Phenotypes of offspring +*m*	*chM*	*ch m*	Recombination and standard error (%)†
I	*ch**+/+$c^{ch(s)}$ × +$c^{ch(s)}$/+$c^{ch(s)}$	31	42	24	26	52.0 ± 7.1
	++/*chp* × *chp*/+*p*	27	26	7	11	46.7 ± 9.1
	*ch**+/+*p* × +*p*/+*p*	5	11	5	7	
II	*ch**+/+*dis* × +*dis*/+*dis*	20	21	12	20	62.5 ± 8.8
III	*ch**+/+*s* × +*s*/+*s*	10	15	8	12	60.0 ± 11.2
	*ch**+/+W^v × ++/++	15	18	9	8	50.0 ± 9.8
	*ch**W^v/++ × ++/++	2	5	5	4	
V	*ch**+/+$a^{(1)}$ × +$a^{(1)}$/+*a*	23	15	16	14	46.0 ± 7.1
	*ch***a*/+*a*^{1} × +*a*/+*a*	9	15	9	11	
	ch+/+*Sd* × *ch*+/++	78	93	16	15	48.4 ± 9.0
VI	*ch***Ca*/++ × ++/++	4	4	4	8	
	*ch**+/+*Ca* × ++/++	23	22	15	15	
	ch+/+*Ca* × *ch*+/++	73	79	8	24	44.2 ± 5.7
	ch Ca/++ × *ch*+/++	11	12		1	
VII	*ch*+/+*Re* × *ch*+/++	61	56	10	15	40.0 ± 10.0
	*ch**+/+*wa-2* × +*wa-2*/+*wa-2*	3	7	5	4	44.5 ± 16.7
VIII	*ch***b*/++ × +*b*/+*b*	12	8	16	4	61.4 ± 7.8
	*ch**+/+*b* × +*b*/+*b*	8	18	11	10	
IX	*ch*+/+*T* × *ch*+/++	144	164	24	38	42.2 ± 6.3‡
	chT/++ × *ch*+/++	1	7		1	
	*ch**+/+*T* × ++/++	11	14	6	14	
X	*ch**+/+*v* × +*v*/+*v*	10	6	5	7	58.3 ± 14.4
XII	*ch**+/+*ru* × +*ru*/+*ru*	35	41	32	20	40.3 ± 6.3
	chru/++ × *chru*/+*ru*	3	..	4	2	
	ch+/+*ru* × *chru*/+*ru*	5	5	3	1	
	*ch**+/+*Io* × +*Io*/+*Io*	28	22	21	9	30.0 ± 9.1
XIII	*ch**+/+*fu* × +*fu*/+*fu*	7	9	7	5	41.7 ± 14.4
	*ch**+/+*ln* × +*ln*/+*ln*	6	4	4	5	55.5 ± 16.7
XIV	*ch**+/+*f* × +*f*/+*f*	10	46	48	3	5.06 (5% fiducial limits 0.93 and 15.72)
	*ch***f*/++ × +*f*/+*f*	7	3	..	1	
	ch+/+*f* × *chf*/+*f*	4	13	6	..	
	ch+/+*f* × *ch*+/+*f*	33	16	14	..	
XX	*ch*♀/+♂ × *ch*♀/+♀	67	54	12	6	66.6 ± 11.8
	ch♂/+♀ × *ch*♀/+♀	110	115	23	11	57.4 ± 6.8

**ch* classified in offspring by genetic test.
†Value calculated from last two columns of data only.
‡Corrected for incomplete penetrance of *T*.

TABLE II. Results of the three-factor linkage tests

Genotype of parents	Phenotypes of offspring							
	+++	*cr*++	++*f*	*cr*+*f*	+*ch*+	*cr*ch+	+*chf*	*cr*ch*f*
+*ch**+/*f*+*cr* × *f*+*cr*/*f*+*cr*	5	4	1	10	18	2	6	..

**ch* classified in offspring by genetic test.

TABLE III. Analysis of data from the three-factor linkage tests

Gene pair	Total	Old combinants	Recombinants	Recombination and standard error (%)
ch, f	26	20	6	23.1 ± 8.4*
ch, cr	26	24	2	7.7 (5% fiducial limits 1.1 and 24.3)*
f, cr	46	33	13	28.0 ± 7.6

*Value calculated from *ch*-carrying offspring only.

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THE INDEX

TO THIS VOLUME HAS BEEN REMOVED FROM THIS POSITION AND PLACED AT THE BEGINNING OF THE FILM FOR THE CONVENIENCE OF READERS.

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1. CARTER, T. C. and D. S. FALCONER. Stocks for detecting linkage and the theory of their design. *Jour. Genet.* 50:307-323. 1951.

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Illustrations: Tables and illustrations should be planned to fit the type-page (5 x 7⅝ inches). Tables should have a descriptive heading. Halftones and line drawings will be accepted in moderate numbers. Drawings must be submitted in a form suitable for cuts. Contributors will be expected to bear half of the cost for excessive numbers of half-tone illustrations. Original photographs should be submitted unmounted in the form of clear black and white prints on glossy paper. Care should be taken to see that they cannot be bent or folded in handling, and paper clips should not be used. All imperfections in the original copy are reproduced.

References: References to the literature should be cited by the author's name and literature cited reference number e.g. (Smith and Jones[5]), or by the number alone where applicable. The bibliography should be arranged alphabetically by author under the heading, *Literature Cited.* Complete reference is necessary and the arrangement should be as follows: Smith, L. C. and C. B. Jones. Inherited skin-defect in cattle. *Jour. Hered.* 32: 419-423. 1941.

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All manuscripts and correspondence should be addressed to the Managing Editor, JOURNAL OF HEREDITY, 1507 M Street, N. W., Washington 5, D. C.

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Its membership is composed of men of science, teachers, publicists, physicians, clergymen, parents, students, horticulturists, and breeders of live stock throughout the world.

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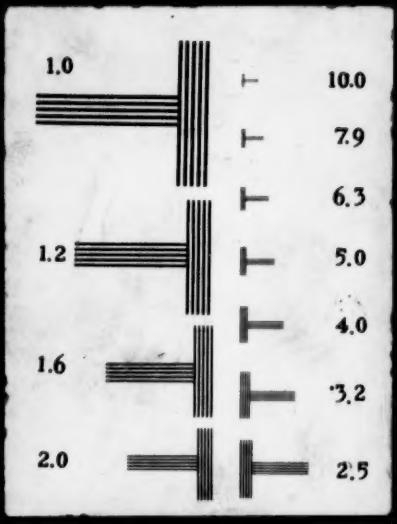
THE AMERICAN GENETIC ASSOCIATION

Washington 5, D. C.

RESOLUTION CHART



100 MILLIMETERS

INSTRUCTIONS Resolution is expressed in terms of the lines per millimeter recorded by a particular film under specified conditions. Numerals in chart indicate the number of lines per millimeter in adjacent "T-shaped" groupings.

In microfilming, it is necessary to determine the reduction ratio and multiply the number of lines in the chart by this value to find the number of lines recorded by the film. As an aid in determining the reduction ratio, the line above is 100 millimeters in length. Measuring this line in the film image and dividing the length into 100 gives the reduction ratio. Example: the line is 20 mm. long in the film image, and 100/20 = 5.

Examine "T-shaped" line groupings in the film with microscope, and note the number adjacent to finest lines recorded sharply and distinctly. Multiply this number by the reduction factor to obtain resolving power in lines per millimeter. Example: 7.9 group of lines is clearly recorded while lines in the 10.0 group are not distinctly separated. Reduction ratio is 5, and 7.9 x 5 = 39.5 lines per millimeter recorded satisfactorily. 10.0 x 5 = 50 lines per millimeter which are not recorded satisfactorily. Under the particular conditions, maximum resolution is between 39.5 and 50 lines per millimeter.

Resolution, as measured on the film, is a test of the entire photographic system, including lens, exposure, processing, and other factors. These rarely utilize maximum resolution of the film. Vibrations during exposure, lack of critical focus, and exposures yielding very dense negatives are to be avoided.